International Application No: PCT/

MICRO	ORGANISMS
Optional Sheet in connection with the microorganism	referred to on page <u>88</u> , lines <u>1-12</u> of the description '
A. IDENTIFICATION OF DEPOSIT	
Further deposits are identified on an additional she	eet *
Name of depositary institution	
American Type Culture Collection	
Address of depositery institution (including post	tal code and country) *
12301 Parklawn Drive	•
Rockville, MD 20852 US	
Date of deposit * May 2, 1991 Accession Num	
B. ADDITIONAL INDICATIONS · (leave blank if not appli	cable). This information is continued on a separate attached aheet
<u> </u>	
C. DESIGNATED STATES FOR WHICH INDICATE	IONS ARE MADE * (# 40 minimum are not all minimum)
D. CEDADATE SURVINIA OF MANAGEMENT	
D. SEPARATE FURNISHING OF INDICATIONS • (I The indications listed below will be submitted to the International *Accession Number of Deposit*)	l Bureau later * (Specify the general nature of the indications e.g.,
·	
E. PThis sheet was received with the International ap	plication when filed (to be checked by the receiving Office)
•	70 0 0
	(Authorized Officer)
☐ The date of receipt (from the applicant) by the I	nternational Bureau "
Was	·
	(Authorized Officer)
Form PCT/RO/134 (January 1981)	

International Application No: PCT/

Form PCT/RO/134 (cont.)

American Type Culture Collection

12301 Parklawn Drive Rockville, MD 20852 US

Accession No.

68609

68611

Date of Deposit

May 2, 1991

May 2, 1991

-89-

SEQUENCE LISTING

(1) GENERAL	INFORMATION:
-------------	--------------

- (i) APPLICANT: Artavanis-Tsakonas, S. et al.
- (ii) TITLE OF INVENTION: Therapeutic And Diagnostic Methods And Compositions Based On Notch Proteins And Nucleic Acids
- (iii) NUMBER OF SEQUENCES: 21
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: Pennie & Edmonds
 - (B) STREET: 1155 Avenue of the Americas
 - (C) CITY: New York
 - (D) STATE: New York
 - (E) COUNTRY: U.S.A.
 - (F) ZIP: 10036
- (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk

 - (B) COMPUTER: IBM PC compatible (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER: To be assigned
 - (B) FILING DATE: On even date
 - (C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: Misrock, S. Leslie

 - (B) REGISTRATION NUMBER: 18,872 (C) REFERENCE/DOCKET NUMBER: 7326-018
 - (ix) TELECOMMUNICATION INFORMATION:

 - (A) TELEPHONE: 212 790-9090 (B) TELEFAX: 212 8698864/9741
 - (C) TELEX: 66141 PENNIE
- (2) INFORMATION FOR SEQ ID NO:1:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2892 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: CDNA
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 142..2640
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

GAATTCGGAG GAATTATTCA AAACATAAAC ACAATAAACA ATTTGAGTAG TTGCCGCACA 60 CACACACA CACAGCCCGT GGATTATTAC ACTAAAAGCG ACACTCAATC CAAAAAATCA 120 GCAACAAAA CATCAATAAA C ATG CAT TGG ATT AAA TGT TTA TTA ACA GCA 171

					-	Met		s Trp	, Ile	Lys 5	Cys	s Lev	Lev	Thi	Ala 10	
					r Val					His					TTT Phe	219
GAC Glu	TT(G CGG	C CTC g Lev 30	Ly:	G TAC	TTC Phe	AGC Ser	AAC Asr 35	n Asp	CAC His	GGC Gly	G CGG 7 Arg	GAC Asp 40) Ası	GAG Glu	. 26
			З Суя					Asp					. TAa		CTG Leu	31!
GC	AGC Ser 60	Cys	C AAC S Lys	ACC Thr	CGG Arg	TTT Phe 65	Arg	GTC Val	TGC Cys	CTA Leu	AAG Lys 70	His	TAC Tyr	CAG Gln	GCC	36:
	Ile					Gln					Asp				Pro 90	411
					Ser					Asp					CAG Gln	459
				Thr					Phe					Ser	TGG Trp	507
			Phe			ATC Ile										555
		Asn			Thr	AAC Asn 145						Arg				603
						TCC Ser										651
						GAG Glu										699
AAC Asn	TAC Tyr	TAC Tyr	GGA Gly 190	TCC Ser	GGC Gly	TGT Cys	GCC Ala	AAG Lys 195	TTC Phe	TGC Cys	CGG Arg	CCC Pro	CGC Arg 200	GAC Asp	GAT Asp	747
						TGC Cys										795
						TAC Tyr 225										843
						GAC Asp					Cys					891
GC	TGG Trp	AAG Lys	GGA Gly	GCC Ala	TTG Leu	TGC Cys	AAC Asn	Glu	TGC Cys	GTT Val	CTG Leu	GAA Glu	CCG Pro	AAC Asn	TGC Cys	939

										•						
				Cys					Thi					Glu	GGT Gly	987
			Le					Asi					Thr		CAC His	1035
		Cys					Thr					Gly			TTG Leu	1083
	Thr					Pro					Asp		_		AAT Asn 330	1131
					Asp					Pro					GGT	1179
				Glu											TGC Cys	1227
GCC	AAC Asn	GGC Gly 365	Trp	AGC Ser	GGA Gly	AAG Lys	ATG Met 370	TGC Cys	GAG Glu	GAG Glu	AAA Lys	GTG Val 375	CTC Leu	ACG Thr	TGT Cys	1275
TCG Ser	GAC Asp 380	Lys	CCC Pro	Cys	CAT His	CAG Gln 385	GGA Gly	ATC Ile	TGC Cys	CGC Arg	AAC Asn 390	GTT Val	CGT Arg	CCT Pro	GGC	1323
												CCC Pro				1371
												AGT Ser				1419
TGC Cys	ATA Ile	AAC Asn	GGT Gly 430	GGA Gly	AGC Ser	TGT Cys	CAG Gln	CCG Pro 435	AGC Ser	GGA Gly	AAG Lys	TGT Cys	ATT Ile 440	TGC Cys	CCA Pro	1467
GCG Ala	GGA Gly	TTT Phe 445	TCG Ser	GGA Gly	ACG Thr	AGA Arg	TGC Cys 450	GAG Glu	ACC	AAC Asn	ATT Ile	GAC Asp 455	GAT Asp	TGT Cys	CTT Leu	1515
GGC Gly	CAC His 460	CAG Gln	TGC Cys	GAG Glu	AAC Asn	GGA Gly 465	GGC Gly	ACC Thr	TGC Cys	ATA Ile	GAT Asp 470	ATG Met	GTC Val	AAC Asn	CAA Gln	1563
												CAC His				1611
												GGA Gly				1659
							Gln.					GCG Ala				1707
	Lys					Asp						AGT Ser 535				1755

CAT His	AAC Asn 540	Gly	GGC	ACT Thr	TGC Cys	ATG Met 545	AAC Asn	CGC Arg	GTC Val	AAT Asn	TCG Ser 550	Phe	GAA Glu	TGC Cys	GTG Val	180	3
TGT Cys 555	Ala	AAT Asn	GGT	TTC Phe	AGG Arg 560	GGC Gly	AAG Lys	CAG Gln	TGC Cys	GAT Asp 565	GAG Glu	GAG Glu	TCC Ser	TAC Tyr	GAT Asp 570	185	1
TCG Ser	GTG Val	ACC	TTC Phe	GAT Asp 575	Ala	CAC His	CAA Gln	TAT Tyr	GGA Gly 580	GCG Ala	ACC Thr	ACA Thr	CAA Gln	GCG Ala 585	AGA Arg	189	9
GCC Ala	GAT Asp	GGT Gly	TTG Leu 590	Thr	AAT Asn	GCC Ala	CAG Gln	GTA Val 595	GTC Val	CTA Leu	ATT Ile	GCT Ala	GTT Val 600	TTC Phe	TCC	194	7
GTT Val	GCG Ala	ATG Met 605	CCT Pro	TTG Leu	GTG Val	GCG Ala	GTT Val 610	ATT Ile	GCG Ala	GCG Ala	TGC Cys	GTG Val 615	GTC Val	TTC Phe	TGC Cys	199	5
ATG Met	AAG Lys 620	CGC Arg	AAG Lys	CGT Arg	AAG Lys	CGT Arg 625	GCT Ala	CAG Gln	GAA Glu	AAG Lys	GAC Asp 630	GAC Asp	GCG Ala	GAG Glu	GCC Ala	204	3
AGG Arg 635	AAG Lys	CAG Gln	AAC Asn	GAA Glu	CAG Gln 640	AAT Asn	GCG Ala	GTG Val	GCC Ala	ACA Thr 645	ATG Met	CAT His	CAC His	AAT Asn	GGC Gly 650	209	1
AGT Ser	GGG Gly	GTG Val	GGT Gly	GTA Val 655	GCT Ala	TTG Leu	GCT Ala	TCA Ser	GCC Ala 660	TCT Ser	CTG Leu	GGC Gly	GGC Gly	AAA Lys 665	ACT Thr	213	9
GGC Gly	AGC Ser	AAC Asn	AGC Ser 670	GGT Gly	CTC Leu	ACC Thr	TTC Phe	GAT Asp 675	GGC Gly	GGC Gly	AAC Asn	CCG Pro	AAT Asn 680	ATC Ile	ATC Ile	218	7
AAA Lys	AAC Asn	ACC Thr 685	TGG Trp	GAC Asp	AAG Lys	TCG Ser	GTC Val 690	AAC Asn	AAC Asn	ATT Ile	TGT Cys	GCC Ala 695	TCA Ser	GCA Ala	GCA Ala	223	5
GCA Ala	GCG Ala 700	GCG Ala	GCG Ala	GCG Ala	GCA Ala	GCA Ala 705	GCG Ala	GCG Ala	GAC Asp	GAG Glu	TGT Cys 710	CTC Leu	ATG Met	TAC Tyr	GGC Gly	. 228	3
GGA Gly 715	TAT Tyr	GTG Val	GCC Ala	TCG Ser	GTG Val 720	GCG Ala	GAT Asp	AAC Asn	AAC Asn	AAT Asn 725	GCC Ala	AAC Asn	TCA Ser	GAC Asp	TTT Phe 730	233	1
TGT Cys	GTG Val	GCT Ala	CCG Pro	CTA Leu 735	CAA Gln	AGA Arg	GCC Ala	AAG Lys	TCG Ser 740	CAA Gln	AAG Lys	CAA Gln	CTC Leu	AAC Asn 745	ACC Thr	237	9
Aab GYL	CCC Pro	ACG Thr	CTC Leu 750	ATG Met	CAC His	CGC Arg	GGT Gly	TCG Ser 755	CCG Pro	GCA Ala	GGC Gly	AGC Ser	TCA Ser 760	GCC Ala	AAG Lys	242	7
GGA Gly	GCG Ala	TCT Ser 765	GGC Gly	GGA Gly	GGA Gly	CCG Pro	GGA Gly 770	GCG Ala	GCG Ala	GAG Glu	GGC Gly	AAG Lys 775	AGG Arg	ATC Ile	TCT Ser	247	5
GTT Val	TTA Leu 780	GGC Gly	GAG Glu	GGT Gly	TCC Ser	TAC Tyr 785	TGT Cys	AGC Ser	CAG Gln	CGT Arg	TGG Trp 790	CCC Pro	TCG Ser	TTG Leu	GCG Ala	252	3
GCG Ala 795	GCG Ala	GGA Gly	GTG Val	GCC Ala	GGA Gly 800	GCC Ala	TGT Cys	TCA Ser	TCC Ser	CAG Gln 805	CTA Leu	ATG Met	GCT Ala	GCA Ala	GCT Ala 810	257:	1

-93-

														TCC Ser 825			2619
GTC Val							TAAC	TCC	A AA	ATCO	CGGAA	G GG	CTC	CTGGI	•		2670
AAAT	CCGG	AG A	AATC	CCGCA	T GO	BAGG	GCTG	ACA	GCAC	ATA	CACA	AAGA	AA i	AGACI	GGG	TT	2730
GGGT	TCAA	AA 1	GTGA	GAGA	G AC	CGCCF	TAAA	GTI	GTTG	TTG	ATTG	AAGC	AG :	TTAG	TCG'	TC	2790
ACGA	AAAA	TG P	AAAA	TCTG	TA	ACAGG	CATA	ACI	CGTA	AAC	TCCC	TAAA	AA I	ATTTG	TAT	AG	2850
TAAT	TAGC	AA A	GCTG	TGAC	C CF	AGCCG	TTTC	GAT	cccg	TAA	TC			-			2892

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 833 amino acids
- (B) TYPE: amino acid.
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met His Trp Ile Lys Cys Leu Leu Thr Ala Phe Ile Cys Phe Thr Val Ile Val Gln Val His Ser Ser Gly Ser Phe Glu Leu Arg Leu Lys Tyr Phe Ser Asn Asp His Gly Arg Asp Asn Glu Gly Arg Cys Cys Ser Gly Glu Ser Asp Gly Ala Thr Gly Lys Cys Leu Gly Ser Cys Lys Thr Arg Phe Arg Val Cys Leu Lys His Tyr Gln Ala Thr Ile Asp Thr Thr Ser Gln Cys Thr Tyr Gly Asp Val Ile Thr Pro Ile Leu Gly Glu Asn Ser Val Asn Leu Thr Asp Ala Gln Arg Phe Gln Asn Lys Gly Phe Thr Asn 105 Pro Ile Gln Phe Pro Phe Ser Phe Ser Trp Pro Gly Thr Phe Ser Leu Ile Val Glu Ala Trp His Asp Thr Asn Asn Ser Gly Asn Ala Arg Thr Asn Lys Leu Leu Ile Gln Arg Leu Leu Val Gln Gln Val Leu Glu Val Ser Ser Glu Trp Lys Thr Asn Lys Ser Glu Ser Gln Tyr Thr Ser Leu 165 170 Glu Tyr Asp Phe Arg Val Thr Cys Asp Leu Asn Tyr Tyr Gly Ser Gly Cys Ala Lys Phe Cys Arg Pro Arg Asp Asp Ser Phe Gly His Ser Thr

Cys Ser Glu Thr Gly Glu Ile Ile Cys Leu Thr Gly Trp Gln Gly Asp Tyr Cys His Ile Pro Lys Cys Ala Lys Gly Cys Glu His Gly His Cys Asp Lys Pro Asn Gln Cys Val Cys Gln Leu Gly Trp Lys Gly Ala Leu Cys Asn Glu Cys Val Leu Glu Pro Asn Cys Ile His Gly Thr Cys Asn Lys Pro Trp Thr Cys Ile Cys Asn Glu Gly Trp Gly Gly Leu Tyr Cys Asn Gln Asp Leu Asn Tyr Cys Thr Asn His Arg Pro Cys Lys Asn Gly Gly Thr Cys Phe Asn Thr Gly Glu Gly Leu Tyr Thr Cys Lys Cys Ala Pro Gly Tyr Ser Gly Asp Asp Cys Glu Asn Glu Ile Tyr Ser Cys Asp Ala Asp Val Asn Pro Cys Gln Asn Gly Gly Thr Cys Ile Asp Glu Pro His Thr Lys Thr Gly Tyr Lys Cys His Cys Ala Asn Gly Trp Ser Gly Lys Met Cys Glu Glu Lys Val Leu Thr Cys Ser Asp Lys Pro Cys His Gln Gly Ile Cys Arg Asn Val Arg Pro Gly Leu Gly Ser Lys Gly Gln 385 Gly Tyr Gln Cys Glu Cys Pro Ile Gly Tyr Ser Gly Pro Asn Cys Asp 405 410 415 Leu Gln Leu Asp Asn Cys Ser Pro Asn Pro Cys Ile Asn Gly Gly Ser Cys Gln Pro Ser Gly Lys Cys Ile Cys Pro Ala Gly Phe Ser Gly Thr Arg Cys Glu Thr Asn Ile Asp Asp Cys Leu Gly His Gln Cys Glu Asn 450 455 460 Gly Gly Thr Cys Ile Asp Met Val Asn Gln Tyr Arg Cys Gln Cys Val 465 470 475 Pro Gly Phe His Gly Thr His Cys Ser Ser Lys Val Asp Leu Cys Leu Ile Arg Pro Cys Ala Asn Gly Gly Thr Cys Leu Asn Leu Asn Asn Asp 500 505 Tyr Gln Cys Thr Cys Arg Ala Gly Phe Thr Gly Lys Asp Cys Ser Val 520 Asp Ile Asp Glu Cys Ser Ser Gly Pro Cys His Asn Gly Gly Thr Cys Met Asn Arg Val Asn Ser Phe Glu Cys Val Cys Ala Asn Gly Phe Arg Gly Lys Gln Cys Asp Glu Glu Ser Tyr Asp Ser Val Thr Phe Asp Ala

WO 94/07474 PCT/US93/09338

-95-

565 570 575

His Gln Tyr Gly Ala Thr Thr Gln Ala Arg Ala Asp Gly Leu Thr Asn 580 585 590

Ala Gln Val Val Leu Ile Ala Val Phe Ser Val Ala Met Pro Leu Val 595 600 605

Ala Val Ile Ala Ala Cys Val Val Phe Cys Met Lys Arg Lys Arg Lys 610 620

Arg Ala Gln Glu Lys Asp Asp Ala Glu Ala Arg Lys Gln Asn Glu Gln 625 630 635 640

Asn Ala Val Ala Thr Met His His Asn Gly Ser Gly Val Gly Val Ala 645 650 655

Leu Ala Ser Ala Ser Leu Gly Gly Lys Thr Gly Ser Asn Ser Gly Leu 660 665 670

Thr Phe Asp Gly Gly Asn Pro Asn Ile Ile Lys Asn Thr Trp Asp Lys 675 680 685

Ala Ala Asp Glu Cys Leu Met Tyr Gly Gly Tyr Val Ala Ser Val 705 710 715 720

Ala Asp Asn Asn Ala Asn Ser Asp Phe Cys Val Ala Pro Leu Gln
725 730 735

Arg Ala Lys Ser Gln Lys Gln Leu Asn Thr Asp Pro Thr Leu Met His 740 745 750

Arg Gly Ser Pro Ala Gly Ser Ser Ala Lys Gly Ala Ser Gly Gly Gly 755 760 765

Pro Gly Ala Ala Glu Gly Lys Arg Ile Ser Val Leu Gly Glu Gly Ser 770 775 780

Tyr Cys Ser Gln Arg Trp Pro Ser Leu Ala Ala Ala Gly Val Ala Gly 785 790 795 800

Ala Cys Ser Ser Gln Leu Met Ala Ala Ala Ser Ala Ala Gly Ser Gly 805 810

Ala Gly Thr Ala Gln Gln Gln Arg Ser Val Val Cys Gly Thr Pro His 820 825 830

Met

(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1320 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 442..1320

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

(X1) SEQUENCE DESCRIPTION. BEQ 15 NO	
CCGAGTCGAG CGCCGTGCTT CGAGCGGTGA TGAGCCC	CCTT TTCTGTCAAC GCTAAAGATC 60
TACAAAACAT CAGCGCCTAT CAAGTGGAAG TGTCAAG	TGT GAACAAACA AAAACGAGAG 120
AAGCACATAC TAAGGTCCAT ATAAATAATA AATAATA	ATT GTGTGTGATA ACAACATTAT 180
CCAAACAAAA CCAAACAAAA CGAAGGCAAA GTGGAGA	AAAA TGATACAGCA TCCAGAGTAC 240
GGCCGTTATT CAGCTATCCA GAGCAAGTGT AGTGTGG	CAA AATAGAAACA AACAAAGGCA 300
CCAAAATCTG CATACATGGG CTAATTAAGG CTGCCCA	AGCG AATTTACATT TGTGTGGTGC 360
CAATCCAGAG TGAATCCGAA ACAAACTCCA TCTAGAT	CGC CAACCAGCAT CACGCTCGCA 420
AACGCCCCCA GAATGTACAA A ATG TTT AGG AAA Met Phe Arg Lys	CAT TTT CGG CGA AAA CCA 471 His Phe Arg Arg Lys Pro 5 10
GCT ACG TCG TCG TCG TTG GAG TCA ACA ATA Ala Thr Ser Ser Ser Leu Glu Ser Thr Ile 15	GAA TCA GCA GAC AGC CTG 519 Glu Ser Ala Asp Ser Leu 25
GGA ATG TCC AAG AAG ACG GCG ACA AAA AGG Gly Met Ser Lys Lys Thr Ala Thr Lys Arg 30	CAG CGT CCG AGG CAT CGG 567 Gln Arg Pro Arg His Arg 40
GTA CCC AAA ATC GCG ACC CTG CCA TCG ACG Val Pro Lys Ile Ala Thr Leu Pro Ser Thr 45	ATC CGC GAT TGT CGA TCA 615 Ile Arg Asp Cys Arg Ser 55
TTA AAG TCT GCC TGC AAC TTA ATT GCT TTA Leu Lys Ser Ala Cys Asn Leu Ile Ala Leu 60 65	ATT TTA ATA CTG TTA GTC 663 Ile Leu Ile Leu Leu Val 70
CAT AAG ATA TCC GCA GCT GGT AAC TTC GAG His Lys Ile Ser Ala Ala Gly Asn Phe Glu 75	CTG GAA ATA TTA GAA ATC 711 Leu Glu Ile Leu Glu Ile 85 90
TCA AAT ACC AAC AGC CAT CTA CTC AAC GGC Ser Asn Thr Asn Ser His Leu Leu Asn Gly 95	TAT TGC TGC GGC ATG CCA 759 Tyr Cys Cys Gly Met Pro 105
GCG GAA CTT AGG GCC ACC AAG ACG ATA GGC Ala Glu Leu Arg Ala Thr Lys Thr 11e Gly 110	TGC TCG CCA TGC ACG ACG 807 Cys Ser Pro Cys Thr Thr 120
GCA TTC CGG CTG TGC CTG AAG GAG TAC CAG Ala Phe Arg Leu Cys Leu Lys Glu Tyr Gln 125	ACC ACG GAG CAG GGT GCC 855 Thr Thr Glu Gln Gly Ala 135
AGC ATA TCC ACG GGC TGT TCG TTT GGC AAC Ser Ile Ser Thr Gly Cys Ser Phe Gly Asn 140	GCC ACC ACC AAG ATA CTG 903 Ala Thr Thr Lys Ile Leu 150
GGT GGC TCC AGC TTT GTG CTC AGC GAT CCG Gly Gly Ser S r Phe Val Leu Ser Asp Pro 155	GGT GTG GGA GCC ATT GTG 951 Gly Val Gly Ala Ile Val 165 170
CTG CCC TTT ACG TTT CGT TGG ACG AAG TCG Leu Pro Phe Thr Phe Arg Trp Thr Lys Ser 175	TTT ACG CTG ATA CTG CAG 999 Phe Thr Leu Il Leu Gln 185
GCG TTG GAT ATG TAC AAC ACA TCC TAT CCA	GAT GCG GAG AGG TTA ATT 1047

WO 94/07474 PCT/US93/09338

-97-

Ala	Leu	Asp	Met 190	Tyr	Asn	Thr	Ser	Tyr 195	Pro	Asp	Ala	Glu	Arg 200	Leu	Ile	
											Ser	CCG Pro 215				1095
												TAC Tyr				1143
												ACG Thr				1191
												GGC Gly				1239
												TGC Cys				1287
								GTC Val						-		1320

(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 293 amino acids

 - (B) TYPE: amino acid (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Met Phe Arg Lys His Phe Arg Arg Lys Pro Ala Thr Ser Ser Leu

Glu Ser Thr Ile Glu Ser Ala Asp Ser Leu Gly Met Ser Lys Lys Thr

Ala Thr Lys Arg Gln Arg Pro Arg His Arg Val Pro Lys Ile Ala Thr

Leu Pro Ser Thr Ile Arg Asp Cys Arg Ser Leu Lys Ser Ala Cys Asn

Leu Ile Ala Leu Ile Leu Ile Leu Leu Val His Lys Ile Ser Ala Ala

Gly Asn Phe Glu Leu Glu Ile Leu Glu Ile Ser Asn Thr Asn Ser His

Leu Leu Asn Gly Tyr Cys Cys Gly Met Pro Ala Glu Leu Arg Ala Thr

Lys Thr Ile Gly Cys Ser Pro Cys Thr Thr Ala Phe Arg Leu Cys Leu 115 120 125

Lys Glu Tyr Gln Thr Thr Glu Gln Gly Ala Ser Ile Ser Thr Gly Cys

Ser Phe Gly Asn Ala Thr Thr Lys Ile Leu Gly Gly Ser Ser Phe Val

145					150		-			155					160
Leu	Ser	Asp	Pro	Gly 165	Val	Gly	Ala	Ile	Val 170	Leu	Pro	Phe	Thr	Phe 175	Arg
Trp	Thr	Lys	Ser 180	Phe	Thr	Leu	Ile	Leu 185	Gln	Ala	Leu	Asp	Met 190	Tyr	Asn
Thr	Ser	Tyr 195	Pro	Asp	Ala	Glu	Arg 200	Leu	Ile	Glu	Glu	Thr 205	ser	Tyr	Ser
Gly	Val 210	Ile	Leu	Pro 	ser	Pro 215	Glu	Trp	Lys	Thr	Leu 220	Asp	His	Ile	Gly
Arg 225	Asn	Ala	Arg	Ile	Thr 230	Tyr	Arg	Val	Arg	Val 235	Gln	Cys	Ala	Val	Thr 240
Tyr	Tyr	Asn	Thr	Thr 245	Cys	Thr	Thr	Phe	Cys 250	Arg	Pro	Arg	Asp	Asp 255	Gln
Phe	Gly	His	Tyr 260	Ala	Cys	Gly	Ser	Glu 265	Gly	Gln	Lys	Leu	Cys 270	Ļeu	Asn
Gly	Trp	Gln 275	Gly	Val	Asn	Cys	Glu 280	Glu	Ala	Ile	Cys	Lys 285	Ala	Gly	Cys
Asp	Pro 290	Val	His	Gly								•			•
(2)	INF	ORMA'	TION	FOR	SEQ	ID :	NO: 5	:						•	
	(i	() ()	A) L B) T C) S	CE C ENGT YPE: TRAN OPOL	H: 2 nuc DEDN	67 b leic ESS:	ase aci dou	paır d ble	s						

(ii) MOLECULE TYPE: CDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5: CGGTGGACTT CCTTCGTGTA TTGGTGGGAG CCCTCGGGAA CGGGGGGTAA CACTGAAAGG 60 TCGAGTACCC ATTTCCGTCA TAACGGGTTG GTCGCCCCCT AGGGGTCGGA GTCAGGTGGA 120 CGGGAGGTCG ACAACGCCCG GGGGACGGGT GGTACATGGT GTAAGGTCTT TACCGGACCG 180 GGCAAACGGG TCACACCGAA AGGGGTGAAC GGTAACTACG GGGTCGTCCT GCCCGTCCAT 240 267 CGAGTCTGGT AAGAGGGTCG CCTTAAG

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 574 base pairs

 - (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: cDNA

٠	(xi)	SE	QUENCE	DESC	CRIPTION:	SI	EQ ID NO:6:				
GAAT	TECTT	C	CATTATA	CGT	GACTTTTCT	G	AAACTGTAGC	CACCCTAGTG	TCTCTAACTC		6
CCTC	TGGAG	T	TTGTCAG	CTT	TGGTCTTTT	C	AAAGAGCAGG	CTCTCTTCAA	GCTCCTTAAT	:	12
GCGG	GCATG	С	TCCAGTI	TGG	TCTGCGTCT	С	AAGATCACCT	TTGGTAATTG	ATTCTTCTTC	;	18
AACC	CGGAA	С	TGAAGGC	TGG	CTCTCACCC	T	CTAGGCAGAG	CAGGAATTCC	GAGGTGGATG	:	24
TGTT	AGATG	T	GAATGTC	CGT	GGCCCAGAT	G	GCTGCACCCC	ATTGATGTTG	GCTTCTCTCC	:	30
GAGG.	AGGCA	G	CTCAGAT	TTG	AGTGATGAA	G	ATGAAGATGC	AGAGGACTGT	TCTGCTAACA	:	360
TCAT	CACAG	A	CTTGGTC	TAC	CAGGGTGCC	A	GCCTCCAGNC	CAGACAGACC	GGACTGGTGA	4	420
GATG	GCCCT	G	CACCTTG	CAG	CCCGCTACT	C	ACGGGCTGAT	GCTGCCAAGC	GTCTCCTGGA	4	480
TGCA	GGTGC	A	GATGCCA	ATG	CCCAGGACAI	Ą	CATGGGCCGC	TGTCCACTCC	ATGCTGCAGT	5	540
GGCA	CGTGA:	r (GCCAAGG	TGT	ATTCAGATC	r	GTTA			5	574
	T117071		DION DO						,	-	

(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 295 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

TCCAGATTCT GATTCGCAAC CGAGTAACTG ATCTAGATGC CAGGATGAAT GATGGTACTA 60
CACCCCTGAT CCTGGCTGC CGCCTGGCTG TGGAGGGAAT GGTGGCAGAA CTGATCAACT 120
GCCAAGCGGA TGTGAATGCA GTGGATGACC ATGGAAAATC TGCTCTTCAC TGGGCAGCTG 180
CTGTCAATAA TGTGGAGGCA ACTCTTTTGT TGTTGAAAAA TGGGGCCAAC CGAGACATGC 240
AGGACAACAA GGAAGAGACA CCTCTGTTC TTGCTGCCCG GGAGGAGCTA TAAGC 295

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 248 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

GAATTCCATT CAGGAGGAAA GGGTGGGGAG AGAAGCAGGC ACCCACTTC CCGTGGCTGG 60
ACTCGTTCCC AGGTGGCTC ACCGGCAGCT GTGACCGCCG CAGGTGGGG CGGAGTGCCA 120
TTCAGAAAAT TCCAGAAAAG CCCTACCCCA ACTCGGACGG CAACGTCACA CCCGTGGGTA 180

-100-

GCAACTGGCA CACAAACAGC CAGCGTGTCT GG	GGCACGGG	GGGATGGCAC	CCCCTGCAGG	240
CAGAGCTG			•	248
(2) INFORMATION FOR SEQ ID NO:9:				
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 323 base pair (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: unknown	:s			
(ii) MOLECULE TYPE: cDNA				
(xi) SEQUENCE DESCRIPTION: SEQ				
TACGTATCTC GAGCACAGAC AGCTGACGTA CA	ACTTTTNNA	GTGCGAGGGA	CATTCGTCCG	60
ACCAGTACGA ACATTTAGGC TCAGTACGGT AC	GGTCCATGG	CCAAGACTAG	GAGACGTAGG	120
GAGCTACAGG TCCCGCTCGC TAAACTCGGA CC	CACTGAAAC	CTCCGGTCGA	CAGTCGGTAA	180
GCGAACAAGA GGGCCAGATC TTAGAGAAGG TO				240
CGGCCTTAAG GACGTCGGGC CCNNNAGGTG AT				300
CGAGGNCGAA AACAAGGGAA ATC				323
(2) INFORMATION FOR SEQ ID NO:10: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 3234 base paids (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: CDNA				
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 13234	vo. 10			
(xi) SEQUENCE DESCRIPTION: SEQ			C ARC ARC	48
TGC CAG GAG GAC GCG GGC AAC AAG GTG Cys Gln Glu Asp Ala Gly Asn Lys Va 1	10	Dea can of	15	
20	5	3	0	96
CCC TGG AAG AAC TGC ACG CAG TCT CT Pro Trp Lys Asn Cys Thr Gln Ser Le 35	G CAG TGC u Gln Cys	TGG AAG TA Trp Lys Ty 45	C TTC AGT or Phe Ser	144
GAC GGC CAC TGT GAC AGC CAG TGC AA Asp Gly His Cys Asp Ser Gln Cys As 50 55	oll Ser wra	60		
GGC TTT GAC TGC CAG CGT GCG GAA GG	C CAG TGC	AAC CCC CI	G TAC GAC	240

-101-

G1 ₃ 65		e Asp	Сув	Gln	Arc 70		Glu	Gly	Gln	Cys 75	Pro	Leu	Tyr	qaA 08	
					His					His				TGC Cys	288
				Cys					Leu				His	GTA Val	336
			Leu										ATG Met	CCG Pro	384
		Gln											CTC Leu	AGC Ser	432
_	Val					Val	_				_		Gly	_	480
													AAG Lys 175		528
													CTG Leu	CTG Leu	576
													GGG Gly		624
													GTC Val		672
													TGC .Cys		720
													TCG Ser 255		768
													GAG Glu		816
													GCG Ala	_	864
										Cys			CTG Leu		912
													GGC Gly		960
AAA Lys													GGC Gly 335		1008

GAC Asp	TCC Ser	GTG Val	GGC Gly 340	CTC Leu	AAG Lys	CCC Pro	CTG Leu	AAG Lys 345	AAC Asn	GCT Ala	TCA Ser	GAC Asp	GGT Gly 350	GCC Ala	CTC Leu	1056
ATG Met	GAC Asp	GAC Asp 355	AAC Asn	CAG Gln	AAT Asn	GAG Glu	TGG Trp 360	GGG Gly	GAC Asp	GAG Glu	GAC Asp	CTG Leu 365	GAG Glu	ACC Thr	AAG Lys	1104
AAG Lys	TTC Phe 370	CGG Arg	TTC Phe	GAG Glu	GAG Glu	CCC Pro 375	GTG Val	GTT Val	CTG Leu	CCT Pro	GAC Asp 380	CTG Leu	GAC Asp	GAC Asp	CAG Gln	1152
ACA Thr 385	GAC Asp	CAC His	CGG Arg	CAG Gln	TGG Trp 390	ACT Thr	CAG Gln	CAG Gln	CAC His	CTG Leu 395	GAT Asp	GCC Ala	GCT Ala	vəħ	CTG Leu 400	1200
CGC Arg	ATG Met	TCT Ser	GCC Ala	ATG Met 405	GCC Ala	CCC Pro	ACA Thr	CCG Pro	CCC Pro 410	CAG Gln	GGT Gly	GAG Glu	GTT Val	GAC Asp 415	GCC Ala	1248
GAC Asp	TGC Cys	ATG Met	GAC Asp 420	GTC Val	AAT Asn	GTC Val	CGC Arg	GGG Gly 425	CCT Pro	GAT Asp	GGC Gly	TTC Phe	ACC Thr 430	CCG Pro	CTC Leu	1296
ATG Met	ATC Ile	GCC Ala 435	TCC Ser	TGC Cys	AGC Ser	GGG Gly	GGC Gly 440	Gly	CTG Leu	GAG Glu	ACG Thr	GGC Gly 445	AAC Asn	AGC Ser	GAG Glu	1344
GAA Glu	GAG Glu 450	GAG Glu	GAC Asp	GCG Ala	CCG Pro	GCC Ala 455	GTC Val	ATC Ile	TCC Ser	GAC Asp	TTC Phe 460	TTE	TAC Tyr	CAG Gln	GGC	1392
GCC Ala 465	AGC Ser	CTG Leu	CAC His	AAC Asn	CAG Gln 470	ACA Thr	GAC Asp	CGC Arg	ACG Thr	GGC Gly 475	GAG Glu	ACC Thr	GCC Ala	TTG Leu	CAC His 480	1440
CTG Leu	GCC Ala	GCC Ala	CGC Arg	TAC Tyr 485	TCA Ser	CGC Arg	TCT Ser	GAT Asp	GCC Ala 490	GCC. Ala	T Aa T	CGC Arg	CTG Leu	CTG Leu 495	GAG Glu	1488
GCC Ala	AGC Ser	GCA Ala	GAT Asp 500	GCC Ala	AAC Asn	ATC Ile	CAG Gln	GAC Asp 505	AAC Asn	ATG Met	GCGC	CGC Arg	ACC Thr 510	CCG Pro	CTG Leu	1536
CAT His	GCG Ala	GCT Ala 515	GTG Val	TCT Ser	GCC Ala	GAC Asp	GCA Ala 520	CAA Gln	GGT Gly	GTC Val	Pne	CAG Gln 525	ATC Ile	CTG Leu	ATC Ile	1584
CGG Arg	AAC Asn 530	CGA Arg	GCC Ala	ACA Thr	GAC Asp	CTG Leu 535	GAT Asp	GCC Ala	CGC Arg	ATG Met	CAT His 540	GAT Asp	GGC Gly	ACG Thr	ACG Thr	1632
CCA Pro 545	CTG Leu	ATC Ile	CTG Leu	GCT Ala	GCC Ala 550	CGC Arg	CTG Leu	GCC Ala	GTG Val	GAG Glu 555	GGC Gly	ATG Met	CTG Leu	GAG Glu	GAC Asp 560	1680
CTC Leu	ATC Ile	AAC Asn	TCA Ser	CAC His 565	GCC Ala	GAC Asp	GTC Val	AAC Asn	GCC Ala 570	GTA Val	GAT Asp	GAC Asp	CTG Leu	GGC Gly 575	AAG Lys	1728
TCC Ser	GCC Ala	CTG Leu	CAC His 580	TGG Trp	GCC Ala	GCC Ala	GCC Ala	GTG Val 585	AAC Asn	AAT Asn	GTG Val	GAT Asp	GCC Ala 590	GCA Ala	GTT Val	1776
GTG Val	CTC Leu	CTG L u 595	AAG Lys	AAC Asn	GGG Gly	GCT Ala	AAC Asn 600	AAA Lys	GAT Asp	ATG Met	CAG Gln	AAC Asn 605	AAC Asn	AGG Arg	GAG Glu	1824

		Pro					Ala					TAC Tyr				-	1872
	. Val					Phe					Ile	ACG Thr					1920
					Asp					Arg		CAT His					1968
GTG Val	AGG Arg	CTG Leu	CTG Leu 660	Asp	GAG Glu	TAC Tyr	AAC Asn	CTG Leu 665	Val	CGC Arg	AGC Ser	CCG Pro	CAG Gln 670	CTG Leu	CAC		2016
			Leu									CCG Pro 685					2064
		Gly										CAG Gln					2112
	Arg											AGC Ser					2160
												GGC Gly					2208
												TCC Ser					2256
												CTG Leu 765					2304
												CTG Leu					2352
	Asp											GCG Ala					2400
												TTT Phe					2448
												ACC Thr					2496
	Gly											GTG Val 845					2544
												CTG Leu					2592
									Arg			GTG Val		Pro			2640

-104-

CCC Pro	CTG Leu	AGC Ser	ACA Thr	CAG Gln 885	GCC Ala	CCC Pro	TCC Ser	CTG Leu	CAG Gln 890	CAT His	GGC Gly	ATG Met	GTA Val	GGC Gly 895	CCG Pro		2688
			AGC Ser 900														2736
CAG Gln	GGC	CTG Leu 915	CCC Pro	AGC Ser	ACC Thr	CGG Arg	CTG Leu 920	GCC Ala	ACC Thr	CAG Gln	CCT Pro	CAC His 925	CTG Leú	GTG Val	CAG Gln		2784
ACC Thr	CAG Gln 930	Gln	GTG Val	CAG Gln	CCA Pro	CAA Gln 935	AAC Asn	TTA Leu	CAG Gln	ATG Met	CAG Gln 940	CAG Gln	CAG Gln	AAC Asn	CTG Leu		2832
CAG Gln 945	Pro	GCA Ala	AAC Asn	ATC Ile	CAG Gln 950	CAG Gln	CAG Gln	CAA Gln	AGC Ser	CTG Leu 955	CAG Gln	CCG Pro	CCA Pro	CCA Pro	CCA Pro 960		2880
CCA Pro	CCA Pro	CAG Gln	CCG Pro	CAC His 965	CTT Leu	GGC Gly	GTG Val	AGC Ser	TCA Ser 970	GCA Ala	GCC Ala	AGC Ser	GGC Gly	CAC His 975	CTG Leu		2928
GGC Gly	CGG Arg	AGC Ser	TTC Phe 980	CTG Leu	AGT Ser	GGA Gly	GAG Glu	CCG Pro 985	AGC Ser	CAG Gln	GCA Ala	GAC Asp	GTG Val 990	CAG Gln	CCA Pro		2976
CTG Leu	GGC Gly	CCC Pro 995	AGC Ser	AGC Ser	CTG Leu	GCG Ala	GTG Val 1000	His	ACT Thr	ATT	CTG Leu	CCC Pro 1005	Gln	GAG Glu	AGC Ser		3024
		Leu	CCC Pro				Pro					Pro					3072
	Ala		TTC Phe			Pro					Ser						3120
			ACC Thr		Ser					Val							3168
			CGA Arg 1060	Ser					Lys					Leu		;	3216
			GAC Asp													;	3234

(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1078 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Cys Gln Glu Asp Ala Gly Asn Lys Val Cys Ser Leu Gln Cys Asn Asn 1 10 15

His Ala Cys Gly Trp Asp Gly Gly Asp Cys Ser Leu Asn Phe Asn Asp Pro Trp Lys Asn Cys Thr Gln Ser Leu Gln Cys Trp Lys Tyr Phe Ser 35 40 45 40 Asp Gly His Cys Asp Ser Gln Cys Asn Ser Ala Gly Cys Leu Phe Asp 50 55 60 Gly Phe Asp Cys Gln Arg Ala Glu Gly Gln Cys Asn Pro Leu Tyr Asp 65 70 75 80 Gln Tyr Cys Lys Asp His Phe Ser Asp Gly His Cys Asp Gln Gly Cys Asn Ser Ala Glu Cys Glu Trp Asp Gly Leu Asp Cys Ala Glu His Val Pro Glu Arg Leu Ala Ala Gly Thr Leu Val Val Val Leu Met Pro Pro Glu Gln Leu Arg Asn Ser Ser Phe His Phe Leu Arg Glu Leu Ser 135 Arg Val Leu His Thr Asn Val Val Phe Lys Arg Asp Ala His Gly Gln Gln Met Ile Phe Pro Tyr Tyr Gly Arg Glu Glu Leu Arg Lys His Pro Ile Lys Arg Ala Ala Glu Gly Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln Val Lys Ala Ser Leu Leu Pro Gly Gly Ser Glu Gly Gly Arg Arg Arg Arg Glu Leu Asp Pro Met Asp Val Arg Gly Ser Ile Val Tyr 210 215 220 Leu Glu Ile Asp Asn Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe 235 Gin Ser Ala Thr Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser Leu Asn Ile Pro Tyr Lys Ile Glu Ala Val Gln Ser Glu Thr Val Glu Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala 280 Ala Ala Phe Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser 295 Arg Lys Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe 310 Lys Val Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg Phe Glu Glu Pro Val Val Leu Pro Asp Leu Asp Asp Gln

WO 94/07474 PCT/US93/09338

-106-

` 370 375 380 Thr Asp His Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu 390 395 Arg Met Ser Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val Asp Ala 410 405 Asp Cys Met Asp Val Asn Val Arg Gly Pro Asp Gly Phe Thr Pro Leu 425 Met Ile Ala Ser Cys Ser Gly Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu Glu Asp Ala Pro Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His 475 Leu Ala Ala Arg Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser Ala Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His Ala Ala Val Ser Ala Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn Arg Ala Thr Asp Leu Asp Ala Arg Met His Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala Arg Leu Ala Val Glu Gly Met Leu Glu Asp Leu Ile Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu Gly Lys 570 Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Asp Ala Ala Val Val Leu Leu Lys Asn Gly Ala Asn Lys Asp Met Gln Asn Asn Arg Glu 600 Glu Thr Pro Leu Phe Leu Ala Ala Arg Glu Gly Ser Tyr Glu Thr Ala 610 615 Lys Val Leu Leu Asp His Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp Ile Ala Gln Glu Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu Tyr Asn Leu Val Arg Ser Pro Gln Leu His Gly Ala Pro Leu Gly Gly Thr Pro Thr Leu Ser Pro Pro Leu Cys Ser 680 Pro Asn Gly Tyr Leu Gly Ser Leu Lys Pro Gly Val Gln Gly Lys Lys 695 Val Arg Lys Pro Ser Ser Lys Gly Leu Ala Cys Gly Ser Lys Glu Ala Lys Asp Leu Lys Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys 730

Leu Leu Asp Ser Ser Gly Met Leu Ser Pro Val Asp Ser Leu Glu Ser 740

Pro His Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Leu Pro Ser 755

Pro Pro Cla Cla Can Dec Can Val Dec Leu Dec Cla Val

Pro Phe Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro Gly Met 770 775 780

Pro Asp Thr His Leu Gly Ile Gly His Leu Asn Val Ala Ala Lys Pro 785 790 795 800

Glu Met Ala Ala Leu Gly Gly Gly Gly Arg Leu Ala Phe Glu Thr Gly 805 810 815

Pro Pro Arg Leu Ser His Leu Pro Val Ala Ser Gly Thr Ser Thr Val 820 825 830

Leu Gly Ser Ser Ser Gly Gly Ala Leu Asn Phe Thr Val Gly Gly Ser 835 840 845

Thr Ser Leu Asn Gly Gln Cys Glu Trp Leu Ser Arg Leu Gln Ser Gly 850 855 860

Met Val Pro Asn Gln Tyr Asn Pro Leu Arg Gly Ser Val Ala Pro Gly 865 870 875 880

Pro Leu Ser Thr Gln Ala Pro Ser Leu Gln His Gly Met Val Gly Pro 885 890 895

Leu His Ser Ser Leu Ala Ala Ser Ala Leu Ser Gln Met Met Ser Tyr 900 905 910

Gln Gly Leu Pro Ser Thr Arg Leu Ala Thr Gln Pro His Leu Val Gln 915 920 925

Thr Gln Gln Val Gln Pro Gln Asn Leu Gln Met Gln Gln Gln Asn Leu 930 935 940

Gln Pro Ala Asn Ile Gln Gln Gln Ser Leu Gln Pro Pro Pro 945 950 955 960

Pro Pro Gln Pro His Leu Gly Val Ser Ser Ala Ala Ser Gly His Leu 965 970 975

Gly Arg Ser Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val Gln Pro 980 985 990

Leu Gly Pro Ser Ser Leu Ala Val His Thr Ile Leu Pro Gln Glu Ser 995 1000 1005

Pro Ala Leu Pro Thr Ser Leu Pro Ser Ser Leu Val Pro Pro Val Thr 1010 1015 1020

Ala Ala Gln Phe Leu Thr Pro Pro Ser Gln His Ser Tyr Ser Ser Pro 1025 1030 1035 1040

Val Asp Asn Thr Pro Ser His Gln Leu Gln Val Pro Val Pro Val Met 1045 1050 1055

Val Met Ile Arg Ser Ser Asp Pro Ser Lys Gly Ser Ser Ile Leu Ile 1060 1065 1070

Glu Ala Pro Asp Ser Trp 1075

(2) INFORMATION FOR SEQ ID NO:12:

PCT/US93/09338 WO 94/07474

-108-

(i)	SEQUENCE	CHAR	ACTE	RISTI	cs:
			4000	1	

- (A) LENGTH: 4268 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS (B) LOCATION: 2..1972

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

	12.	_,	- 2	.02 -							- •						
			GAT (Asp \				_										46
					Ala					Gly					AGT Ser		94
	_			Asp					Ser					Thr	GAC Asp	1	.42
			Gln					Gln					Arg		GGT	1	90
		: Ala					Ala					Ala			GCC Ala	. 2	38
AAG Lys 80	Arg	CTC Leu	CTG Leu	GAT Asp	GCA Ala 85	Gly	GCA Ala	GAT Asp	GCC	AAT Asn 90	Ala	CAG Gln	GAC Asp	AAC Asn	ATG Met 95	2 ;	86
			CCA Pro													3	34
			CTG Leu 115													38	82
			ACT Thr													43	30
			GCA Ala													47	78
			GGA Gly													52	26
_			ACT Thr													. 57	4
			AAG Lys 195				Pro									62	2

-109-

			ı Ala					Lev					Ası		GAC Asp	670
		Ası					Leu					Ala			CGC Arg	718
	: His					Arg					Tyr				Pro 255	766
					. Val	TTG Leu									Cys	814
				Ser		CTC Leu			Lys					Gly	AAG Lys	862
			Arg			GCC Ala							Ser			910
AAC	Leu 305	Ala	AAG Lys	GAG Glu	GCA Ala	AAG Lys 310	GAT Asp	GCC Ala	AAG Lys	GGT Gly	AGT Ser 315	AGG Arg	AGG Arg	AAG Lys	AAG Lys	958
TCT Ser 320	Leu	AGT Ser	GAG Glu	AAG Lys	GTC Val 325	CAA Gln	CTG Leu	TCT Ser	GAG Glu	AGT Ser 330	TCA Ser	GTA Val	ACT	TTA Leu	TCC Ser 335	1006
						TCT Ser										1054
						TCC Ser										1102
						GCC Ala										1150
						CTT Leu 390										1198
						TCA Ser										1246
						GGC										1294
						GAT Asp										1342
						TTT Phe										1390
						CCC Pro 470				Pro						1438

PCT/US93/09338

-110-

WO 94/07474

ATA ACC ACC CCT CGG GAG CCC TTG CCC CCC ATT GTG ACT TTC CAG CTC Ile Thr Thr Pro Arg Glu Pro Leu Pro Pro Ile Val Thr Phe Gln Leu 480 485 490 495	1486
ATC CCT AAA GGC AGT ATT GCC CAA CCA GCG GGG GCT CCC CAG CCT CAG Ile Pro Lys Gly Ser Ile Ala Gln Pro Ala Gly Ala Pro Gln Pro Gln 500 505 510	1534
TCC ACC TGC CCT CCA GCT GTT GCG GGC CCC CTG CCC ACC ATG TAC CAG Ser Thr Cys Pro Pro Ala Val Ala Gly Pro Leu Pro Thr Met Tyr Gln 515 520 525	1582
ATT CCA GAA ATG GCC CGT TTG CCC AGT GTG GCT TTC CCC ACT GCC ATG Ile Pro Glu Met Ala Arg Leu Pro Ser Val Ala Phe Pro Thr Ala Met 530 540	1630
ATG CCC CAG CAG GAC GGG CAG GTA GCT CAG ACC ATT CTC CCA GCC TAT Met Pro Gln Gln Asp Gly Gln Val Ala Gln Thr Ile Leu Pro Ala Tyr 545 550 555	1678
CAT CCT TTC CCA GCC TCT GTG GGC AAG TAC CCC ACA CCC CCT TCA CAG His Pro Phe Pro Ala Ser Val Gly Lys Tyr Pro Thr Pro Pro Ser Gln 560 565 570 575	1726
CAC AGT TAT GCT TCC TCA AAT GCT GCT GAG CGA ACA CCC AGT CAC AGT His Ser Tyr Ala Ser Ser Asn Ala Ala Glu Arg Thr Pro Ser His Ser 580 585 590	1774
GGT CAC CTC CAG GGT GAG CAT CCC TAC CTG ACA CCA TCC CCA GAG TCT Gly His Leu Gln Gly Glu His Pro Tyr Leu Thr Pro Ser Pro Glu Ser 595 600 605	1822
CCT GAC CAG TGG TCA AGT TCA TCA CCC CAC TCT GCT TCT GAC TGG TCA Pro Asp Gln Trp Ser Ser Ser Pro His Ser Ala Ser Asp Trp Ser 610 615 620	1870
GAT GTG ACC ACC CCT ACC CCT GGG GGT GCT GGA GGA GGT CAG CGG Asp Val Thr Thr Ser Pro Thr Pro Gly Gly Ala Gly Gly Gln Arg 625 630 635	1918
GGA CCT GGG ACA CAC ATG TCT GAG CCA CCA CAC AAC AAC ATG CAG GTT Gly Pro Gly Thr His Met Ser Glu Pro Pro His Asn Asn Met Gln Val 640 655	1966
TAT GCG TGAGAGAGTC CACCTCCAGT GTAGAGACAT AACTGACTTT TGTAAATGCT Tyr Ala	2022
GCTGAGGAAC AAATGAAGGT CATCCGGGAG AGAAATGAAG AAATCTCTGG AGCCAGCTTC	2082
TAGAGGTAGG AAAGAGAAGA TGTTCTTATT CAGATAATGC AAGAGAAGCA ATTCGTCAGT	2142
TTCACTGGGT ATCTGCAAGG CTTATTGATT ATTCTAATCT AATAAGACAA GTTTGTGGAA	2202
ATGCAAGATG AATACAAGCC TTGGGTCCAT GTTTACTCTC TTCTATTTGG AGAATAAGAT	2262
GGATGCTTAT TGAAGCCCAG ACATTCTTGC AGCTTGGACT GCATTTTAAG CCCTGCAGGC	2322
TTCTGCCATA TCCATGAGAA GATTCTACAC TAGCGTCCTG TTGGGAATTA TGCCCTGGAA	2382
TTCTGCCTGA ATTGACCTAC GCATCTCCTC CTCCTTGGAC ATTCTTTTGT CTTCATTTGG	2442
TGCTTTTGGT TTTGCACCTC TCCGTGATTG TAGCCCTACC AGCATGTTAT AGGGCAAGAC	2502
CTTTGTGCTT TTGATCATTC TGGCCCATGA AAGCAACTTT GGTCTCCTTT CCCCTCCTGT	2562
CTTCCCGGTA TCCCTTGGAG TCTCACAAGG TTTACTTTGG TATGGTTCTC AGCACAAACC	2622

•	TTTCAAGTAT	GTTGTTTCT1	TGGAAAATGG	ACATACTGTA	TTGTGTTCTC	CTGCATATAT	2682
(CATTCCTGG	GAGAGAAGGG	GAGAAGAATA	CTTTTCTTCA	ACAAATTTTG	GGGGCAGGAG	2742
i	ATCCCTTCAP	GAGGCTGCAC	CTTAATTTTT	CTTGTCTGTG	TGCAGGTCTT	CATATAAACT	2802
•	TTACCAGGAA	GAAGGGTGTG	AGTTTGTTGT	TTTTCTGTGT	ATGGGCCTGG	TCAGTGTAAA	2862
(GTTTTATCCI	TGATAGTCTA	GTTACTATGA	CCCTCCCCAC	TTTTTTAAAA	CCAGAAAAAG	2922
(GTTTGGAATG	TTGGAATGAC	CAAGAGACAA	GTTAACTCGT	GCAAGAGCCA	GTTACCCACC	2982
(CACAGGTCCC	CCTACTTCCT	GCCAAGCATT	CCATTGACTG	CCTGTATGGA	ACACATTTGT	3042
(CCCAGATCTG	AGCATTCTAG	GCCTGTTTCA	CTCACTCACC	CAGCATATGA	AACTAGTCTT	3102
2	AACTGTTGAG	CCTTTCCTTT	CATATCCACA	GAAGACACTG	TCTCAAATGT	TGTACCCTTG	3162
(CCATTTAGGA	CTGAACTTTC	CTTAGCCCAA	GGGACCCAGT	GACAGTTGTC	TTCCGTTTGT	3222
C	CAGATGATCA	GTCTCTACTG	ATTATCTTGC	TGCTTAAAGG	CCTGCTCACC	AATCTTTCTT	3282
7	rcacaccgtg	TGGTCCGTGT	TACTGGTATA	CCCAGTATGT	TCTCACTGAA	GACATGGACT	3342
3	TATATGTTC	AAGTGCAGGA	ATTGGAAAGT	TGGACTTGTT	TTCTATGATC	CAAAACAGCC	3402
c	TATAAGAAG	GTTGGAAAAG	GAGGAACTAT	ATAGCAGCCT	TTGCTATTTT	CTGCTACCAT	3462
1	TCTTTTCCT	CTGAAGCGGC	CATGACATTC	CCTTTGGCAA	CTAACGTAGA	AACTCAACAG	3522
A	ACATTTTCC	TTTCCTAGAG	TCACCTTTTA	GATGATAATG	GACAACTATA	GACTTGCTCA	3582
T	TGTTCAGAC	TGATTGCCCC	TCACCTGAAT	CCACTCTCTG	TATTCATGCT	CTTGGCAATT	3642
T	CTTTGACTT	TCTTTTAAGG	GCAGAAGCAT	TTTAGTTAAT	TGTAGATAAA	GAATAGTTTT	3702
C	TTCCTCTTC	TCCTTGGGCC	AGTTAATAAT	TGGTCCATGG	CTACACTGCA	ACTTCCGTCC	3762
A	GTGCTGTGA	TGCCCATGAC	ACCTGCAAAA	TAAGTTCTGC	CTGGGCATTT	TGTAGATATT	3822
A	ACAGGTGAA	TTCCCGACTC	TTTTGGTTTG	AATGACAGTT	CTCATTCCTT	CTATGGCTGC	3882
A	AGTATGCAT	CAGTGCTTCC	CACTTACCTG	ATTTGTCTGT	CGGTGGCCCC	ATATGGAAAC	3942
C	CTGCGTGTC	TGTTGGCATA	ATAGTTTACA	AATGGTTTTT	TCAGTCCTAT	CCAAATTTAT	4002
T	Gaaccaaca	AAAATAATTA	CTTCTGCCCT	GAGATAAGCA	GATTAAGTTT	GTTCATTCTC	4062
T	GCTTTATTC	TCTCCATGTG	GCAACATTCT	GTCAGCCTCT	TTCATAGTGT	GCAAACATTT	4122
T	ATCATTCTA	AATGGTGACT	CTCTGCCCTT	GGACCCATTT	ATTATTCACA	GATGGGGAGA	4182
A	CCTATCTGC	ATGGACCCTC	ACCATCCTCT	GTGCAGCACA	CACAGTGCAG	GGAGCCAGTG	4242
G	CGATGGCGA	TGACTTTCTT	CCCCTG				4268

(2) INFORMATION FOR SEQ ID NO:13:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 657 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

Glu Val Asp Val Leu Asp Val Asn Val Arg Gly Pro Asp Gly Cys Thr Pro Leu Met Leu Ala Ser Leu Arg Gly Gly Ser Ser Asp Leu Ser Asp Glu Asp Glu Asp Ala Glu Asp Ser Ser Ala Asn Ile Ile Thr Asp Leu Val Tyr Gln Gly Ala Ser Leu Gln Ala Gln Thr Asp Arg Thr Gly Glu Met Ala Leu His Leu Ala Ala Arg Tyr Ser Arg Ala Asp Ala Ala Lys
65 70 75 80 Arg Leu Leu Asp Ala Gly Ala Asp Ala Asn Ala Gln Asp Asn Met Gly Arg Cys Pro Leu His Ala Ala Val Ala Ala Asp Ala Gln Gly Val Phe 105 Gln Ile Leu Ile Arg Asn Arg Val Thr Asp Leu Asp Ala Arg Met Asn Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala Arg Leu Ala Val Glu Gly Met Val Ala Glu Leu Ile Asn Cys Gln Ala Asp Val Asn Ala Val Asp Asp His Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Glu Ala Thr Leu Leu Leu Lys Asn Gly Ala Asn Arg Asp Met Gln 185 Asp Asn Lys Glu Glu Thr Pro Leu Phe Leu Ala Ala Arg Glu Gly Ser 200 Tyr Glu Ala Ala Lys Ile Leu Leu Asp His Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp Val Ala Arg Asp Arg Met 230 His His Asp Ile Val Arg Leu Leu Asp Glu Tyr Asn Val Thr Pro Ser Pro Pro Gly Thr Val Leu Thr Ser Ala Leu Ser Pro Val Ile Cys Gly 265 Pro Asn Arg Ser Phe Leu Ser Leu Lys His Thr Pro Met Gly Lys Lys 280 Ser Arg Arg Pro Ser Ala Lys Ser Thr Met Pro Thr Ser Leu Pro Asn Leu Ala Lys Glu Ala Lys Asp Ala Lys Gly Ser Arg Arg Lys Lys Ser Leu Ser Glu Lys Val Gln Leu Ser Glu Ser Ser Val Thr Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His Thr Tyr Val Ser Asp Thr Thr S r 345 Ser Pro Met Ile Thr Ser Pro Gly Ile Leu Gln Ala Ser Pro Asn Pro

365 355 360 Met Leu Ala Thr Ala Ala Pro Pro Ala Pro Val His Ala Gln His Ala 375 Leu Ser Phe Ser Asn Leu His Glu Met Gln Pro Leu Ala His Gly Ala 395 390 Ser Thr Val Leu Pro Ser Val Ser Gln Leu Leu Ser His His His Ile 410 405 Val Ser Pro Gly Ser Gly Ser Ala Gly Ser Leu Ser Arg Leu His Pro Val Pro Val Pro Ala Asp Trp Met Asn Arg Met Glu Val Asn Glu Thr Gln Tyr Asn Glu Met Phe Gly Met Val Leu Ala Pro Ala Glu Gly Thr 455 His Pro Gly Ile Ala Pro Gln Ser Arg Pro Pro Glu Gly Lys His Ile Thr Thr Pro Arg Glu Pro Leu Pro Pro Ile Val Thr Phe Gln Leu Ile Pro Lys Gly Ser Ile Ala Gln Pro Ala Gly Ala Pro Gln Pro Gln Ser 505 Thr Cys Pro Pro Ala Val Ala Gly Pro Leu Pro Thr Met Tyr Gln Ile Pro Glu Met Ala Arg Leu Pro Ser Val Ala Phe Pro Thr Ala Met Met 535 Pro Gln Gln Asp Gly Gln Val Ala Gln Thr Ile Leu Pro Ala Tyr His Pro Phe Pro Ala Ser Val Gly Lys Tyr Pro Thr Pro Pro Ser Gln His Ser Tyr Ala Ser Ser Asn Ala Ala Glu Arg Thr Pro Ser His Ser Gly His Leu Gln Gly Glu His Pro Tyr Leu Thr Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Pro His Ser Ala Ser Asp Trp Ser Asp Val Thr Thr Ser Pro Thr Pro Gly Gly Ala Gly Gly Gln Arg Gly 630 Pro Gly Thr His Met Ser Glu Pro Pro His Asn Asn Met Gln Val Tyr 650 645

(2) INFORMATION FOR SEQ ID NO:14:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 77 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown

Ala

- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Glu Asp Ile Asp Glu Cys Asp Gln Gly Ser Pro Cys Glu His Asn Gly
1 10 175

Ile Cys Val Asn Thr Pro Gly Ser Tyr Arg Cys Asn Cys Ser Gln Gly 20 25 30

Phe Thr Gly Pro Arg Cys Glu Thr Asn Ile Asn Glu Cys Glu Ser His 35 40 45

Pro Cys Gln Asn Glu Gly Ser Cys Leu Asp Asp Pro Gly Thr Phe Arg 50 60

Cys Val Cys Met Pro Gly Phe Thr Gly Thr Gln Cys Glu 65 70 75

- (2) INFORMATION FOR SEQ ID NO:15:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 78 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Asn Asp Val Asp Glu Cys Ser Leu Gly Ala Asn Pro Cys Glu His Gly
1 10 15

Gly Arg Cys Thr Asn Thr Leu Gly Ser Phe Gln Cys Asn Cys Pro Gln
20 25 30

Gly Tyr Ala Gly Pro Arg Cys Glu Ile Asp Val Asn Glu Cys Leu Ser 35 40 45

Asn Pro Cys Gln Asn Asp Ser Thr Cys Leu Asp Gln Ile Gly Glu Phe 50 60

Gln Cys Ile Cys Met Pro Gly Tyr Glu Gly Leu Tyr Cys Glu 65 70 75

- (2) INFORMATION FOR SEQ ID NO:16:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 654 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Thr Pro Pro Gln Gly Glu Ile Glu Ala Asp Cys Met Asp Val Asn Val

1				5					10					15	
Arg	Gly	Pro	Asp 20	Gly	Phe	Thr	Pro	Leu 25	Met	Ile	Ala	Ser	Cys 30	Ser	Gļ
Gly	Gly	Leu 35	Glu	Thr	Gly	Asn	Ser 40	Glu	Glu	Glu	Glu	Asp 45	Ala	ser	Ala
Asn	Met 50	Ile	Ser	Asp	Phe	Ile 55	Gly	Gln	Gly	Ala	Gln 60	Leu	His	Asn	Gli
Thr 65	Asp	Arg	Thr	Ģly	Glu 70	Thr	Ala	Leu	His	Leu 75	Ala	Ala	Arg	Tyr	A18
Arg	Ala	Asp	Ala	Ala 85	Lys	Arg	Leu	Leu	Glu 90	Ser	Ser	Ala	Asp	Ala 95	Ası
Val	Gln	Asp	Asn 100	Met	Gly	Arg	Thr	Pro 105	Leu	His	Ala	Ala	Val 110	Ala	Ala
Asp	Ala	Gln 115	Gly	Val	Phe	Gln	Ile 120	Leu	Ile	Arg	Asn	Arg 125	Ala	Thr	Asj
Leu	Asp 130	Ala	Arg	Met	Phe	Asp 135	Gly	Thr	Thr	Pro	Leu 140	Ile	Leu	Ala	Ala
Arg 145	Leu	Ala	Val	Glu	Gly 150	Met	Val	Glu	Glu	Leu 155	Ile	Asn	Ala	His	Ala 160
Asp	Val	Asn	Ala	Val 165	Asp	Glu	Phe	Gly	Lys 170	Ser	Ala	Leu	His	Trp 175	Ala
Ala	Ala	Val	Asn 180	Asn	Val	Asp	Ala	Ala 185	Ala	Val	Leu	Leu	Lys 190	Asn	Sei
Ala		Lys 195	Asp	Met	Gln	Asn	Asn 200	Lys	Glu	Glu	Thr	Ser 205	Leu	Phe	Leu
Ala	Ala 210	Arg	Glu	Gly	Ser	Tyr 215	Glu	Thr	Ala	Lys	Val 220	Leu	Leu	Asp	His
Tyr 225	Ala	Asn	Arg	Asp	11e 230	Thr	Asp	His	Met	Asp 235	Arg	Leu	Pro	Arg	Asg 240
Ile	Ala	Gln	Glu	Arg 245	Met	His	His	Asp	Ile 250	Val	His	Leu	Leu	Asp 255	Glu
-			Val 260					265			٠		270		
		275	Ser				280					285			
Met	Lys 290	Pro	Ser	Val	Gln	Ser 295	Lys	Lys	Ala	Arg	300	Pro	Ser	Ile	Lys
Gly 305	Asn	Gly	Cys	Lys	Glu 310	Ala	Lys	Glu	Leu	Lys 315	Ala	Arg	Arg	Lys	120 320
Ser	Gln	Asp	Gly	Lys 325	Thr	Thr	Leu	Leu	Asp 330	Ser	Gly	Ser	Ser	Gly 335	Va]
			Val 340	_				345	•				350		
Val		Ser 355	Pro	Pro	Leu	Met	Thr 360	Ser	Pro	Phe	Gln	Gln 365	s r	Pro	Ser

PCT/US93/09338 WO 94/07474

-116-

Met Pro Leu Asn His Leu Thr Ser Met Pro Glu Ser Gln Leu Gly Met Asn His Ile Asn Met Ala Thr Lys Gln Glu Met Ala Ala Gly Ser Asn Arg Met Ala Phe Asp Ala Met Val Pro Arg Leu Thr His Leu Asn Ala Ser Ser Pro Asn Thr Ile Met Ser Asn Gly Ser Met His Phe Thr Val Gly Gly Ala Pro Thr Met Asn Ser Gln Cys Asp Trp Leu Ala Arg Leu 435 Gln Asn Gly Met Val Gln Asn Gln Tyr Asp Pro Ile Arg Asn Gly Ile Gln Gln Gly Asn Ala Gln Gln Ala Gln Ala Leu Gln His Gly Leu Met Thr Ser Leu His Asn Gly Leu Pro Ala Thr Thr Leu Ser Gln Met Met Thr Tyr Gln Ala Met Pro Asn Thr Arg Leu Ala Asn Gln Pro His Leu Met Gln Ala Gln Gln Met Gln Gln Gln Asn Leu Gln Leu His Gln 520 Ser Met Gln Gln His His Asn Ser Ser Thr Thr Ser Thr His Ile 535 Asn Ser Pro Phe Cys Ser Ser Asp Ile Ser Gln Thr Asp Leu Gln Gln Met Ser Ser Asn Asn Ile His Ser Val Met Pro Gln Asp Thr Gln Ile 570 Phe Ala Ala Ser Leu Pro Ser Asn Leu Thr Gln Ser Met Thr Thr Ala Gln Phe Leu Thr Pro Pro Ser Gln His Ser Tyr Ser Ser Pro Met Asp 600 605 Asn Thr Pro Ser His Gln Leu Gln Val Pro Asp His Pro Phe Leu Thr Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Pro His Ser Asn Met Ser Asp Trp Ser Glu Gly Ile Ser Ser Pro Pro Thr 645

(2) INFORMATION FOR SEQ ID NO:17:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 666 amino acids

 - (B) TYPE: amino acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Thr Pro Pro Gln Gly Glu Val Asp Ala Asp Cys Met Asp Val Asn Val Arg Gly Pro Asp Gly Phe Thr Pro Leu Met Ile Ala Ser Cys Ser Gly Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu Glu Asp Ala Pro Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His Leu Ala Ala Arg Tyr Ser Arg 65 70 75 80 Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser Ala Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His Ala Ala Val Ser Ala Asp 105 Ala Cln Gly Val Phe Gln Ile Leu Leu Arg Asn Arg Ala Thr Asp Leu 120 Asp Ala Arg Met His Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala Arg Leu Ala Val Glu Gly Met Leu Glu Asp Leu Ile Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Asp Ala Ala Val Val Leu Leu Lys Asn Gly Ala Asn Lys Asp Met Gln Asn Asn Lys Glu Glu Thr Pro Leu Phe Leu Ala Ala Arg Glu Gly Ser Tyr Glu Thr Ala Lys Val Leu Leu Asp His Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp Ile 235 Ala Gln Glu Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu Tyr 250 Asn Leu Val Arg Ser Pro Gln Leu His Gly Thr Ala Leu Gly Gly Thr 260 265 270 265 Pro Thr Leu Ser Pro Thr Leu Cys Ser Pro Asn Gly Tyr Leu Gly Asn 275 280 285 Leu Lys Ser Ala Thr Gln Gly Lys Lys Ala Arg Lys Pro Ser Thr Lys Gly Leu Ala Cys Ser Ser Lys Glu Ala Lys Asp Leu Lys Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys Leu Leu Asp Ser Ser Ser Met Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Pro S r Pro Phe Gln Gln Ser Pro Ser Met

-118-

		355	5				360)				365	5		
Pro	370		His	Leu	Pro	Gly 375		Pro	Asp	Thr	His 380		Gly	Ile	Ser
His 385) Asr	Val	. Ala	Ala 390		Pro	Glu	Met	Ala 395		Leu	Ala	Gly	Gly 400
Ser	Arç	J Lev	Ala	Phe 405		Pro	Pro	Pro	Pro 410		Leu	Ser	His	Leu 415	Pro
Val	Ala	Ser	Ser 420		Ser	Thr	Val	Leu 425		Thr	Asn	Gly	Thr 430		Ala
Met	Asn	Phe 435		Val	Gly	Ala	Pro 440		Ser	Leu	Asn	Gly 445		Cys	Glu
Trp	Leu 450		Arg	Leu	Gln	Asn 455	Gly	Met	Val	Pro	Ser 460	Gln	Tyr	Asn	Pro
Leu 465		Pro	Gly	Val	Thr 470	Pro	Gly	Thr	Leu	Ser 475	Thr	Gln	Ala	Ala	Gly 480
Leu	Gln	His	Gly	Met 485	Met	Ser	Pro	Ile	His 490	Ser	Ser	Leu	Ser	Thr 495	Asn
Thr	Leu	Ser	Pro 500	Ile	Ile	Tyr	Gln	Gly 505	Leu	Pro	Asn	Thr	Arg 510	Leu	Ala
Thr	Gln	Pro 515	His	Leu	Val	Gln	Thr 520	Gln	Gln	Val		Pro 525	Gln	Asn	Leu
Gln	Ile 530	Gln	Pro	Gln	Asn	Leu 535	Gln	Pro	Pro	Ser	Gln 540	Pro	His	Leu	Ser
Val 545	Ser	Ser	Ala	Ala	Asn 550	Gly	His	Leu	Gly	Arg 555	Ser	Phe	Leu	Ser	Gly 560
Glu	Pro	Ser	Gln	Ala 565	Asp	Val	Gln	Pro	Leu 570	Gly	Pro	Ser	Ser	Leu 575	Pro
Val	His	Thr	11e 580	Leu	Pro	Gln	Glu	Ser 585	Gln	Ala	Leu	Pro	Thr 590	Ser	Leu
Pro	Ser	Ser 595	Met	Val	Pro	Pro	Met 600	Thr	Thr	Thr	Gln	Phe 605	Leu	Thr	Pro '
	Ser 610	Gln	His	Ser	Tyr	Ser 615		Ser	Pro		Asp 620		Thr	Pro	Ser
lis 525	Gln	Leu	Gln	Val	Pro 630	Glu	His	Pro	Phe	Leu 635	Thr	Pro	Ser		Glu 640
Ser	Pro	Asp		Trp 645	Ser	Ser	Ser		Arg 650	His	Ser	Asn	Ile	Ser 655	Asp
rp	Ser	Glu	Gly 660	Ile	Ser	Ser		Pro 665	Thr			•			

(2) INFORMATION FOR SEQ ID NO:18:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 681 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18: Thr Pro Pro Gln Gly Glu Val Asp Ala Asp Cys Met Asp Val Asn Val Arg Gly Pro Asp Gly Phe Thr Pro Leu Met Ile Ala Ser Cys Ser Gly Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu Glu Asp Ala Pro Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His Leu Ala Ala Arg Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser Ala Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His Ala Ala Val Ser Ala Asp 105 Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn Arg Ala Thr Asp Leu Asp Ala Arg Met His Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala Arg 135 Leu Ala Val Glu Gly Met Leu Glu Asp Leu Ile Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Asp Ala Ala Val Leu Leu Lys Asn Gly Ala 185 Asn Lys Asp Met Gln Asn Asn Arg Glu Glu Thr Pro Leu Phe Leu Ala Ala Arg Glu Gly Ser Tyr Glu Thr Ala Lys Val Leu Leu Asp His Phe 215 Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp Ile
225 230 235 240 Ala Gln Glu Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu Tyr Asn Leu Val Arg Ser Pro Gln Leu His Gly Ala Pro Leu Gly Gly Thr Pro Thr Leu Ser Pro Pro Leu Cys Ser Pro Asn Gly Tyr Leu Gly Ser Leu Lys Pro Gly Val Gln Gly Lys Lys Val Arg Lys Pro Ser Ser Lys 290 . 295 300 Gly Leu Ala Cys Gly Ser Lys Glu Ala Lys Asp Leu Lys Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys Leu Leu Asp Ser Ser Gly Met

					32	5				33	0				339	5
Le	eu Se	er P	ro	Va. 34		p Se	r Le	u Gl	u Se: 34!		o His	s Gly	у Туз	250 350		. Asp
Va	1 A1		er 55	Pro	o Pr	o Le	u Le	u Pr		r Pro) Phe	e Glr	Glr 365		Pro	Ser
Va	1 Pr 37		eu	Ası	n Hi	s Le	u Pr 37		y Met	t Pro	Asp	380		. Leu	ı Gly	Ile
G1 38		s L	eu	Ası	ı Va	1 Ala 390		a Ly	s Pro	Glu	Met 395		Ala	Lev	Gly	Gly 400
Gl	y Gl	уА	rg	Let	409		e Gl	u Thi	r Gly	/ Pro 410		Arg	Leu	Ser	His 415	Leu
Pr	o Va	1 A	la	Ser 420		/ Thi	Se	r Thi	425		Gly	Ser	Ser	Ser 430		Gly
Al	a Le		sn 35	Phe	Thi	· Val	l Gly	y Gly 440		Thr	Ser	Leu	Asn 445		Gln	Cya
Gl	45		eu	Ser	Arç	g Lev	Gl: 455		Gly	Met	Val	Pro 460		Gln	Tyr	Asn
Pro 46	D Le	u Ai	g	Gly	Ser	Val 470		a Pro	Gly	Pro	Leu 475	Ser	Thr	Gln	Ala	Pro 480
Se	. Le	u G)	n	His	Gly 485		Va]	l Gly	Pro	Leu 490		Ser	Ser	Leu	Ala 495	Ala
Sea	Ala	a Le	eu	Ser 500		Met	Met	: Ser	Tyr 505		Gly	Leu	Pro	Ser 510	Thr	Arg
Let	a Ala	3 Th 51		Gln	Pro	His	Leu	Val 520		Thr	Gln	Gln	Val 525	Gln	Pro	Gln
Asr	530		n :	Met	Gl'n	Gln	Gln 535		Leu	Gln	Pro	Ala 540	Asn	Ile	Gln	Gln
Gln 545		s Se	r:	Leu	Gln	Pro 550	Pro	Pro	Pro	Pro	Pro 555	Gln	Pro	His	Leu	Gly 560
Val	Ser	Se	ri	Ala	Ala 565	Ser	Gly	His	Leu	Gly 570	Arg	Ser	Phe	Leu	Ser 575	Gly
Glu	Pro	Se.		31n 580		Asp	Val		Pro 585		Gly	Pro	Ser	Ser 590	Leu .	Ala
Val	His	Th: 59		lle	Leu	Pro	Gln	Glu 600	Ser	Pro	Ala	Leu	Pro 605	Thr	Ser	Leu
Pro	Ser 610		r I	Leu	Val	Pro	Pro 615	Val	Thr	Ala		Gln 620	Phe	Leu	Thr	Pro
Pro 625	Ser	Glı	a F	lis	Ser	Tyr 630	Ser	Ser	Pro	Val	Glu 635	Asn	Thr	Pro	Ser	His 640
Gln	Leu	Glr	ı V	'al	Pro 645	Glu	His	Pro	Phe	Leu 650	Thr	Pro	Ser	Pro	Glu 655	Ser
Pro	Asp	Glr		rp 60	Ser	Ser	Ser	Ser	Pro 665	His	Ser .	Asn '		Ser 670	Asp '	Trp
Ser	Glu	Gly 675		al	Ser	Ser	Pro	Pro 680	Thr							

(2) INFORMATION FOR SEQ ID NO:19:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2471 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:
- Met Pro Ala Leu Arg Pro Ala Leu Leu Trp Ala Leu Leu Ala Leu Trp 1 5 10 15
- Leu Cys Cys Ala Ala Pro Ala His Ala Leu Gln Cys Arg Asp Gly Tyr
 20 25 30
- Glu Pro Cys Val Asn Glu Gly Met Cys Val Thr Tyr His Asn Gly Thr
 35 40 45
- Gly Tyr Cys Lys Cys Pro Glu Gly Phe Leu Gly Glu Tyr Cys Gln His 50 55 60
- Arg Asp Pro Cys Glu Lys Asn Arg Cys Gln Asn Gly Gly Thr Cys Val 65 70 75 80
- Ala Gln Ala Met Leu Gly Lys Ala Thr Cys Arg Cys Ala Ser Gly Phe 85 90 95
- Thr Gly Glu Asp Cys Gln Tyr Ser Thr Ser His Pro Cys Phe Val Ser 100 105 110
- Arg Pro Cys Leu Asn Gly Gly Thr Cys His Met Leu Ser Arg Asp Thr 115 120 125
- Tyr Glu Cys Thr Cys Gln Val Gly Phe Thr Gly Lys Glu Cys Gln Trp 130 135 140
- Thr Asp Ala Cys Leu Ser His Pro Cys Ala Asn Gly Ser Thr Cys Thr 145 150 155 160
- Thr Val Ala Asn Gln Phe Ser Cys Lys Cys Leu Thr Gly Phe Thr Gly 165 170 175
- Gln Lys Cys Glu Thr Asp Val Asn Glu Cys Asp Ile Pro Gly His Cys 180 185 190
- Gln His Gly Gly Thr Cys Leu Asn Leu Pro Gly Ser Tyr Gln Cys Gln 195 200 205
- Cys Pro Gln Gly Phe Thr Gly Gln Tyr Cys Asp Ser Leu Tyr Val Pro 210 215 220
- Cys Ala Pro Ser Pro Cys Val Asn Gly Gly Thr Cys Arg Gln Thr Gly 225 230 235 240
- Asp Phe Thr Phe Glu Cys Asn Cys Leu Pro Gly Phe Glu Gly Ser Thr 245 250 255
- Cys Glu Arg Asn Ile Asp Asp Cys Pro Asn His Arg Cys Gln Asn Gly 260 265 270
- Gly Val Cys Val Asp Gly Val Asn Thr Tyr Asn Cys Arg Cys Pro Pro 275 280 285

Gln	Trp 290	Thr	Gly	Gln	Phe	Cys 295	Thr	Glu	Asp	Val	Asp 300	Glu	Cys	Leu	Leu
Gln 305	Pro	Asn	Ala	Cys	Gln 310	Asn	Gly	Gly	Thr	Cys 315	Ala	Asn	Arg	Asn	Gly 320
Gly	Tyr	Gly	Cys	Val 325	Cys	Val	Asn	Gly	Trp 330	Ser	Gly	Asp	Asp	Cys 335	Ser
Glu	Asn	Ile	Asp 340	Asp	Cys	Ala	Phe	Ala 345	Ser	Cys	Thr	Pro	Gly 350	Ser	Thr
Cys	Ile	Asp 355	Arg	Val	Ala	Ser	Phe 360	Ser	Cys	Met	Cys	Pro 365	Glu	Gly	Lys
Ala	Gly 370	Leu	Leu	Cys	His	Leu 375	Asp	Asp	Ala	Cys	11e 380	Ser	Asn	Pro	Cys
His 385	Lys	Gly	Ala	Leu	Cys 390	Asp	Thr	Asn	Pro	Leu 395	Asn	Gly	Gln	Tyr	11e 400
Сув	Thr	Cys	Pro	Gln 405	Gly	Tyr	Lys	Gly	Ala 410	Asp	Cys	Thr	Glu	Asp 415	Val
Asp	Glu	Cys	Ala 420	Met	Ala	Asn	Ser	Asn 425	Pro	Cys	Glu	His	Ala 430	Gly	Lys
Сув	Val	Asn 435	Thr	Asp	Gly	Ala	Phe 440	His	Cys	Glu	Cys	Leu 445	Lys	Gly	Tyr
	450				Glu	455					460				
465					Thr 470					475					480
	_			485	Phe				490					495	
			500		Pro			505					510		
		515			Cys		520					525			
_	530				Asp	535					540				
545					His 550					555			-		200
				565	Leu				570					575	
_		_	580		Gly			585		•			590		
Cys	Ile	Cys 595	Asn	Pro	Gly	Tyr	Met 600	Gly	Ala	Ile	Cys	Ser 605	Asp	Gln	Ile
_	610	_			Ser	615					620				Asp
625					Gln 630					635					640
Asn	Cys	Glu	Ile	Asn	Phe	Asp	Asp	Cys	Ala	Ser	Asn	Pro	Cys	Ile	His

				645	5				650	0				655	i
Gly	y Ilo	е Су	s Me		Gly	y Ile	e Asr	Arg 665		r Ser	Cys	s Val	Cys 670		Pro
Gly	y Phe	e Th:		y Glr	Arç	Cy:	8 Asr 680		e yal	, Ile	e Asp	685		Ala	Ser
Ası	690		a Ar	g Lys	Gly	Ala 695		Cys	Ile	e Asn	Gl _y 700		. Asn	Gly	Phe
Arg 705		s Ile	e Cys	Pro	Glu 710		/ Pro	His	His	715		Cys	Tyr	Ser	Gln 720
Val	. Asr	ı Glu	ı Cys	. 725		Asr	Pro	Cys	11∈ 730		Gly	' Asn	Сув	735	Gly
Gly	Leu	ser	Gly 740		Lys	Сув	Leu	Cys 745		Ala	Gly	Trp	Val 750		Ile
Asn	Сув	755		. Asp	Lys	Asn	760		Leu	Ser	Asn	Pro 765	Сув	Gln	Asn
Gly		Thr		Asp	Asn	Leu 775		Asn	Gly	Tyr	Arg 780		Thr	Cys	Lys
Lys 785			Lys	Gly	Tyr 790	Asn	Cys	Gln	Val	Asn 795	Ile	Asp	Glu	Cys	Ala 800
Ser	Asn	Pro	Cys	Leu 805	Asn	Gln	Gly	Thr	Cys 810		Asp	Asp	Ile	Ser 815	Gly
Tyr	Thr	Cys	His 820	Cys	Val	Leu	Pro	Tyr 825	Thr	Gly	Lys	Asn	Cys 830	Gln	Thr
Val	Leu	Ala 835		Cys	Ser	Pro	Asn 840	Pro	Cys	Glu	Asn	Ala 845	Ala	Val	Cys
Lys	Glu 850	Ser	Pro	Asn	Phe	Glu 855	Ser	Tyr	Thr	Cys	Leu 860	Cys	Ala	Pro	Gly
Trp 865	Gln	Gly	Gln	Arg	Cys 870	Thr	Ile	Asp	Ile	Asp 875	Glu	Cys	Ile	Ser	Lys 880
Pro	Cys	Met	Asn	His 885	Gly	Leu	Cys	His	Asn 890	Thr	Gln	Gly	Ser	Tyr 895	Met
Cys	Glu	Cys	Pro 900	Pro	Gly	Phe		Gly 905		Asp	Cys	Glu	Glu 910	Asp	Ile
Asp	Asp	Cys 915	Leu	Ala	Asn	Pro	Cys 920	Gln	Asn	Gly	Gly	Ser 925	Cys	Met	Asp
Gly	Val 930	Asn	Thr	Phe	Ser	Cys 935	Leu	Cys	Leu	Pro	Gly 940	Phe	Thr	Gly	Asp
Lys 945	Cys	Gln	Thr	Asp	Met 950	Asn	Glu	Cys	Leu	Ser 955	Glu	Pro	Cys	Lys	Asn 960
3ly	Gly	Thr	Cys	Ser 965	Asp	Tyr	Val		Ser 970	Tyr	Thr	Cys	Lys	Cys 975	Gln
Ala	Gly	Phe	Asp 980	Gly	Val	His	-	Glu 985	Asn	Asn	Ile		Glu 990	Cys	Thr
lu		Ser 995	Cys	Phe	Asn		Gly 1000		Cys	Val		Gly 1005		Asn	Ser

- Phe Ser Cys Leu Cys Pro Val Gly Phe Thr Gly Ser Phe Cys Leu His 1010 1015 1020
- Glu Ile Asn Glu Cys Ser Ser His Pro Cys Leu Asn Glu Gly Thr Cys 1025 1030 1035 1040
- Val Asp Gly Leu Gly Thr Tyr Arg Cys Ser Cys Pro Leu Gly Tyr Thr 1045 1050 1055
- Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser Arg Ser Pro Cys 1060 1065 1070
- Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln Cys Leu 1075 1080 1085
- Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn Val Ser 1090 1095 1100
- Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His Leu Cys 1105 1115 1120
- Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr Cys Gln 1125 1130 1135
- Cys Pro Leu Gly Tyr Thr Gly Ser Tyr Cys Glu Glu Gln Leu Asp Glu 1140 1150
- Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp Phe Ile 1155 1160 1165
- Gly Gly Tyr Arg Cys Glu Cys Val Pro Gly Tyr Gln Gly Val Asn Cys 1170 1175 1180
- Glu Tyr Glu Val Asp Glu Cys Gln Asn Gln Pro Cys Gln Asn Gly Gly 1185 1190 1195 1200
- Thr Cys Ile Asp Leu Val Asn His Phe Lys Cys Ser Cys Pro Pro Gly 1205 1210 1215
- Thr Arg Gly Leu Cys Glu Glu Asn Ile Asp Asp Cys Ala Arg Gly 1220 1225 1230
- Pro His Cys Leu Asn Gly Gly Gln Cys Met Asp Arg Ile Gly Gly Tyr 1235 1240 1245
- Ser Cys Arg Cys Leu Pro Gly Phe Ala Gly Glu Arg Cys Glu Gly Asp 1250 1255 1260
- Ile Asn Glu Cys Leu Ser Asn Pro Cys Ser Ser Glu Gly Ser Leu Asp 1265 1270 1275 1280
- Cys Ile Gln Leu Thr Asn Asp Tyr Leu Cys Val Cys Arg Ser Ala Phe 1285 1290 1295
- Thr Gly Arg His Cys Glu Thr Phe Val Asp Val Cys Pro Gln Met Pro 1300 1305 1310
- Cys Leu Asn Gly Gly Thr Cys Ala Val Ala Ser Asn Met Pro Asp Gly 1315 1320 1325
- Phe Ile Cys Arg Cys Pro Pro Gly Phe Ser Gly Ala Arg Cys Gln Ser 1330 1335 1340
- Ser Cys Gly Gln Val Lys Cys Arg Lys Gly Glu Gln Cys Val His Thr 1345 1350 1355 1360
- Ala Ser Gly Pro Arg Cys Phe Cys Pro Ser Pro Arg Asp Cys Glu Ser

-125-

				136	55				137	70				137	5
Gly	Cys	a Ala	a Sei 138		Pro	Cys	s Glr	138		, Gly	ser Ser	Cys	139		Gln
Arg	Glr	139		Туг	Туг	: Ser	Cys 140		Cys	Ala	Pro	Pro 140		e Ser	Gly
Ser	Arc 141		3 Glu	Leu	Туг	Thr 141		Pro	Pro) Ser	Thr 142		Pro	Ala	Thr
Cys 142		Ser	: Glr	Tyr	Cys 143		Asp	Lys	Ala	Arg 143		Gly	Val	Cys	Asp 1440
Glu	Ala	Сув	s Asr	Ser 144		Ala	Cys	Gln	Trp 145		Gly	Gly	Asp	Cys 145	
Leu	Thr	Met	Glu 146		Pro	Trp	Ala	Asn 146		Ser	Ser	Pro	Leu 147	Pro 0	Cys
Trp	Asp	Tyr 147		: Asn	Asn	Gln	Cys 148		Glu	Leu	Cys	Asn 148		Val	Glu
Cys	Leu 149		Asp	Asn	Phe	Glu 149		Gln	Gly	Asn	Ser 150		Thr	Cys	Lys
Tyr 150		Lys	Tyr	Сув	Ala 151	_	His	Phe	Lys	Asp 151		His	Cys	Asn	Gln 1520
Gly	Cys	Asn	Ser	Glu 152		Cys	Gly	Trp	Asp 153		Leu	Asp	Cys	Ala 153	
Asp	Gln	Pro	Glu 154		Leu	Ala	Glu	Gly 154		Leu	Val	Ile	Val 155	Val 0	Leu
Met	Pro	Pro 155		Gln	Leu	Leu	Gln 156	-	Ala	Arg	Ser	Phe 156		Arg	Ala
Leu	Gly 157		Leu	Leu	His	Thr 157		Leu	Arg	Ile	Lys 1580		Asp	Ser	Gln
Gly 1585		Leu	Met	Val	Tyr 159		Tyr	Tyr	Gly	Glu 1595		Ser	Ala	Ala	Met 1600
Lys	Lys	Gln	Arg	Met 160		Arg	Arg	Ser	Leu 1610		Gly	Glu	Gln	Glu 1615	Gln ·
Glu	Val	Ala	Gly 1620		Lys	Val	Phe	Leu 1629		Ile	Asp	Asn	Arg 1630	Gln)	Cys
/al	Gln	Asp 163		Asp	His	Cys	Phe 1640		Asn	Thr	Asp	Ala 1645		Ala	Ala
	Leu 1650		Ser	His	Ala	11e 1655		Gly	Thr	Leu	Ser 1660	_	Pro	Leu	Val
Ser 1665		Val	Ser	Glu	Ser 1670		Thr	Pro	Glu	Arg 1675		Gln	Leu	Leu	Tyr 1680
Leu	Leu	Ala	Val	Ala 1685		Val	Ile	Ile	Leu 1690		Ile	Ile	Leu	Leu 1695	
/al	Ile	Met	Ala 1700		Arg	Lys	Arg	Lys 1705		Gly	Ser	Leu	Trp 1710	Leu :	Pro
lu		Phe 1715		Leu	Arg	Arg	Asp 1720		Ser	Asn		Lys 1725		Arg	Glu

- Pro Val Gly Gln Asp Ala Val Gly Leu Lys Asn Leu Ser Val Gln Val 1730 1735 1740
- Ser Glu Ala Asn Leu Ile Gly Thr Gly Thr Ser Glu His Trp Val Asp 1745 1750 1755 1760
- Asp Glu Gly Pro Gln Pro Lys Lys Val Lys Ala Glu Asp Glu Ala Leu 1765 1770 1775
- Leu Ser Glu Glu Asp Asp Pro Ile Asp Arg Arg Pro Trp Thr Gln Gln 1780 1785 1790
- His Leu Glu Ala Ala Asp Ile Arg Arg Thr Pro Ser Leu Ala Leu Thr 1795 1800 1805
- Pro Pro Gln Ala Glu Gln Glu Val Asp Val Leu Asp Val Asn Val Arg 1810 1815 1820
- Gly Pro Asp Gly Cys Thr Pro Leu Met Leu Ala Ser Leu Arg Gly Gly
 1825 1830 1835 1840
- Ser Ser Asp Leu Ser Asp Glu Asp Glu Asp Ala Glu Asp Ser Ser Ala 1845 1850 1855
- Asn Ile Ile Thr Asp Leu Val Tyr Gln Gly Ala Ser Leu Gln Ala Gln 1860 1865 1870
- Thr Asp Arg Thr Gly Glu Met Ala Leu His Leu Ala Ala Arg Tyr Ser 1875 1880 1885
- Arg Ala Asp Ala Ala Lys Arg Leu Leu Asp Ala Gly Ala Asp Ala Asn 1890 1895
- Ala Gln Asp Asn Met Gly Arg Cys Pro Leu His Ala Ala Val Ala Ala 1905 1910 1915 1920
- Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn Arg Val Thr Asp 1925 1930 1935
- Leu Asp Ala Arg Met Asn Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala 1940 1945 1950
- Arg Leu Ala Val Glu Gly Met Val Ala Glu Leu Ile Asn Cys Gln Ala 1955 1960 1965
- Asp Val Asn Ala Val Asp Asp His Gly Lys Ser Ala Leu His Trp Ala 1970 1975 1980
- Ala Ala Val Asn Asn Val Glu Ala Thr Leu Leu Leu Leu Lys Asn Gly
 1985 1990 1995
- Ala Asn Arg Asp Met Gln Asp Asn Lys Glu Glu Thr Pro Leu Phe Leu 2005 2010 2015
- Ala Ala Arg Glu Gly Ser Tyr Glu Ala Ala Lys Ile Leu Leu Asp His 2020 2025 2030
- Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp 2035 2040 2045
- Val Ala Arg Asp Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu 2050 2055 2060
- Tyr Asn Val Thr Pro Ser Pro Pro Gly Thr Val Leu Thr Ser Ala Leu 2065 2070 2075 2080
- Ser Pro Val Ile Cys Gly Pro Asn Arg Ser Phe Leu Ser Leu Lys His

							•	-127-	-						
				208	35				209	90				209	5
Th	r Pr	o Me	t Gly 210		E Ly	s Se	r Arg	210		Ser	Ala	Lys	Ser 211		Met
Pro	o Thi	21		Pro	Ası	n Le	a Ala 212		Glu	Ala	Lys	Asp 212		Lys	Gly
Se	21:		J Lys	Lys	s Sez	213		Glu	Lys	. Val	Gln 214		Ser	Glu	Ser
Sei 214		l Thi	r Leu	Ser	Pro 215		l Asp	Ser	Leu	Glu 215		Pro	His	Thr	Tyr 2160
Va]	l Ser	. Yel) Thr	Thr 216		Ser	Pro	Met	11e 217	Thr 0	Ser	Pro	Gly	Ile 217	
Glr	n Ala	ser	Pro 218		Pro	Met	: Leu	Ala 218		Ala	Ala	Pro	Pro 219		Pro
Val	His	219		His	Ala	Leu	Ser 220		Ser	Asn	Leu	His 220		Met	Gln
Pro	Leu 221		His	Gly	Ala	Ser 221		Val	Leu	Pro	Ser 222		Ser	Gln	Leu
Leu 222		His	His	His	11e 223		Ser	Pro	Gly	Ser 223		Ser.	Ala	Gly	Ser 2240
Leu	Ser	Arg	Leu	His 224		Val	Pro	Val	Pro 225	Ala O	Asp	Trp	Met	Asn 2255	
Met	Glu	Val	Asn 226		Thr	Gln	Tyr	Asn 226		Met	Phe	Gly	Met 227		Leu
Ala	Pro	Ala 227		Gly	Thr	His	Pro 228		Ile	Ala	Pro	Gln 2285		Arg	Pro
Pro	Glu 229		Lys	His	Ile	Thr 229		Pro	Arg	Glu	Pro 2300		Pro	Pro	Ile
Val 230	Thr 5	Phe	Gln	Leu	1le 231		Lys	Gly	Ser	Ile 2315		Gln	Pro	Ala	Gly 2320
Ala	Pro	Gln	Pro	Gln 2329		Thr	Cys	Pro	Pro 2330	Ala)	Val	Ala	Gly	Pro 2335	
Pro	Thr	Met	Tyr 2340		Ile	Pro	Glu	Met 2345		Arg	Leu		ser 2350		Ala
Phe	Pro	Thr 235		Met	Met	Pro	Gln 2360		Asp	Gly		Val 2365		Gln	Thr
Ile	Leu 2370		Ala	Tyr	His	Pro 2375		Pro	Ala	Ser	Val 2380		Lys	Tyr	Pro
Thr 2385		Pro	Ser	Gln	His 2390		Tyr	Ala	Ser	Ser 2395		Ala	Ala		Arg 2400
Thr	Pro	Ser	His	Ser 2405		His	Leu		Gly 2410	Glu :	His	Pro		Leu 2415	Thr
Pro	Ser	Pro	Glu 2420		Pro	Asp		Trp 2425		Ser	Ser		Pro 2430		Ser
Ala	Ser	Asp 2435		Ser	Asp	Val	Thr 2440		Ser	Pro '		Pro (Gly	Gly i	Ala

Gly Gly Gln Arg Gly Pro Gly Thr His Met Ser Glu Pro Pro His 2450 2455 2460

Asn Asn Met Gln Val Tyr Ala 2465 2470

(2) INFORMATION FOR SEQ ID NO:20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2556 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:
- Met Pro Pro Leu Leu Ala Pro Leu Leu Cys Leu Ala Leu Leu Pro Ala 1 5 10 15
- Leu Ala Ala Arg Gly Pro Arg Cys Ser Gln Pro Gly Glu Thr Cys Leu 20 25 30
- Asn Gly Gly Lys Cys Glu Ala Ala Asn Gly Thr Glu Ala Cys Val Cys 35 40 45
- Gly Gly Ala Phe Val Gly Pro Arg Cys Gln Asp Pro Asn Pro Cys Leu 50 55
- Ser Thr Pro Cys Lys Asn Ala Gly Thr Cys His Val Val Asp Arg Arg 65 70 75 80
- Gly Val Ala Asp Tyr Ala Cys Ser Cys Ala Leu Gly Phe Ser Gly Pro 85 90 95
- Leu Cys Leu Thr Pro Leu Asp Asn Ala Cys Leu Thr Asn Pro Cys Arg 100 105 110
- Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg 115 120 125
- Cys Pro Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys 130 135 140
- Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ala 145 150 150 160
- Ser Tyr Ile Cys His Cys Pro Pro Ser Phe His Gly Pro Thr Cys Arg 165 170 175
- Gln Asp Val Asn Glu Cys Gly Gln Lys Pro Arg Leu Cys Arg His Gly 180 185 190
- Gly Thr Cys His Asn Glu Val Gly Ser Tyr Arg Cys Val Cys Arg Ala 195 200 205
- Thr His Thr Gly Pro Asn Cys Glu Arg Pro Tyr Val Pro Cys Ser Pro 210 215 220
- Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr 225 230 235 240
- His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu 245 250 255

Asn Ile Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn 300 Ala Cys Gln Asn Gly Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys 405 Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Pro Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe Gin Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu 535 Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly 550 555 Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser 595 600 Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala

	610					615					620		•		
Tyr 625	Leu	Cys	Phe	Cys	Leu 630	Lys	Gly	Thr	Thr	Gly 635	Pro	Asn	Cys	Glu	11e 640
Asn	Leu	Asp	Asp	Cys 645	Ala	Ser	Ser	Pro	Cys 650	Asp	Ser	Gly	Thr	Cys 655	Leu
Asp	Lys	Ile	Asp 660	Gly	Tyr	Glu	Cys	Ala 665	Cys	Glu	Pro	Gly	Tyr 670	Thr	Gly
		Cys 675					680					685			
Asn	Gly G90	Gly	Thr	Cys	Glu	Asp 695	Gly	Ile	Asn	Gly	Phe 700	Thr	Cys	Arg	Сув
Pro 705	Glu	Gly	Tyr	His	Asp 710	Pro	Thr	Cys	Leu	Ser 715	Glu	Val	Asn	Glu	Cys 720
naA	Ser	Asn	Pro	Cys 725	Val	His	Gly	Ala	Cys 730	Arg	Asp	Ser	Leu	Asn 735	Gly
Tyr	Lys	Cys	Asp 740	Cys	Asp	Pro	Gly	Trp 745	Ser	Gly	Thr	Asn	Cys 750	Asp	Ile
Asn		Asn 755		Cys	Glu	Ser	Asn 760	Pro	Cys	Val	Asn	Gly 765	Gly	Thr	Cys
Lys	Asp 770	Met	Thr	Ser	Gly	Ile 775	Val	Cys	Thr	Cys	Arg 780	Glu	Gly	Phe	Ser
Gly 785	Pro	Asn	Cya	Gln	Thr 790	Asn	Ile	Asn	Glu	Cys 795	Ala	Ser	Asn	Pro	Cys 800
Leu	Asn	Lys	Gly	Thr 805	Cys	Ile	Asp	Asp	Val 810	Ala	Gly	Tyr	Lys	Cys 815	Asn
Cys	Leu	Leu	Pro 820	Tyr	Thr	Gly	Ala	Thr 825	Cys	Glu	Val	Val	Leu 830	Ala	Pro
Cys	Ala	Pro 835	Ser	Pro	Cys	Arg	Asn 840	Gly.	Gly	Glu	Cys	Arg 845	Gln	Ser	Glu
	850	Glu				855					860				
Gln 865	Thr	Cys	Glu	Val	Asp 870	Ile	Asn	Glu	Cys	Val 875	Leu	Ser	Pro	Cys	Arg 880
His	Gly	Ala	Ser	Cys 885	Gln	Asn	Thr	His	Gly 890	Gly	Tyr	Arg	Cys	His 895	Cys
Gln	Ala	Gly	Tyr 900	Ser	Gly	Arg	Asn	Cys 905	Glu	Thr	Asp	Ile	Asp 910	Asp	Cys
Arg	Pro	Asn 915	Pro	Сла	His	Asn	Gly 920	Gly	Ser	Cys	Thr	Asp 925	Gly	Ile	Asn
Thr	Ala 930	Phe	Cys	Asp	Cys	Leu 935	Pro	Gly	Phe	Arg	Gly 940	Thr	Phe	Cys	Glu
Glu 945	Asp	Ile	Asn	Glu	Cys 950	Ala	Ser	Asp	Pro	Cys 955	Arg	Asn	Gly	Ala	Asn 960
Cys	Thr	Asp	Cys	Val 965	Asp	Ser	Tyr	Thr	Cys 970	Thr	Cys	Pro	Ala	Gly 975	Phe

WO 94/07474 PCT/US93/09338

Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser 980 985 990

Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys 995 1000 1005

Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val Asn 1010 1015 1020

Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln Asp Gly 1025 1030 1035 1040

Arg Gly Leu His Arg Cys Thr Cys Pro Gln Gly Tyr Thr Gly Pro Asn 1045 1050 1055

Cys Gln Asn Leu Val His Trp Cys Asp Ser Ser Pro Cys Lys Asn Gly 1060 1065 1070

Gly Lys Cys Trp Gln Thr His Thr Gln Tyr Arg Cys Glu Cys Pro Ser 1075 1080 1085

Gly Trp Thr Gly Leu Tyr Cys Asp Val Pro Ser Val Ser Cys Glu Val 1090 1095 1100

Ala Ala Gln Arg Gln Gly Val Asp Val Ala Arg Leu Cys Gln His Gly 1105 1110 1115

Gly Leu Cys Val Asp Ala Gly Asn Thr His His Cys Arg Cys Gln Ala 1125 1130 1135

Gly Tyr Thr Gly Ser Tyr Cys Glu Asp Leu Val Asp Glu Cys Ser Pro 1140 1145 1150

Ser Pro Cys Gln Asn Gly Ala Thr Cys Thr Asp Tyr Leu Gly Gly Tyr 1155 1160 1165

Ser Cys Lys Cys Val Ala Gly Tyr His Gly Val Asn Cys Ser Glu Glu 1170 . 1175 1180

Ile Asp Glu Cys Leu Ser His Pro Cys Gln Asn Gly Gly Thr Cys Leu 1185 1190 1195 1200

Asp Leu Pro Asn Thr Tyr Lys Cys Ser Cys Pro Arg Gly Thr Gln Gly 1205 1210 1215

Val His Cys Glu Ile Asn Val Asp Asp Cys Asn Pro Pro Val Asp Pro 1220 1225 1230

Val Ser Arg Ser Pro Lys Cys Phe Asn Asn Gly Thr Cys Val Asp Gln 1235 1240 1245

Val Gly Gly Tyr Ser Cys Thr Cys Pro Pro Gly Phe Val Gly Glu Arg 1250 1255 1260

Cys Glu Gly Asp Val Asn Glu Cys Leu Ser Asn Pro Cys Asp Ala Arg 1265 1270 1275 1280

Gly Thr Gln Asn Cys Val Gln Arg Val Asn Asp Phe His Cys Glu Cys 1285 1290 1295

Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val Ile Asn Gly Cys 1300 1305 1310

Lys Gly Lys Pro Cys Lys Asn Gly Gly Thr Cys Ala Val Ala Ser Asn 1315 1320 1325

Thr Ala Arg Gly Phe Ile Cys Lys Cys Pro Ala Gly Phe Glu Gly Ala

1340 1335 1330 Thr Cys Glu Asn Asp Ala Arg Thr Cys Gly Ser Leu Arg Cys Leu Asn 1355 1350 Gly Gly Thr Cys Ile Ser Gly Pro Arg Ser Pro Thr Cys Leu Cys Leu 1375 1370 1365 Gly Pro Phe Thr Gly Pro Glu Cys Gln Phe Pro Ala Ser Ser Pro Cys 1385 1380 Leu Gly Gly Asn Pro Cys Tyr Asn Gln Gly Thr Cys Glu Pro Thr Ser Glu Ser Pro Phe Tyr Arg Cys Leu Cys Pro Ala Lys Phe Asn Gly Leu 1420 1415 Leu Cys His Ile Leu Asp Tyr Ser Phe Gly Gly Gly Ala Gly Arg Asp 1435 1430 Ile Pro Pro Pro Leu Ile Glu Glu Ala Cys Glu Leu Pro Glu Cys Gln 1450 Glu Asp Ala Gly Asn Lys Val Cys Ser Leu Gln Cys Asn Asn His Ala 1465 Cys Gly Trp Asp Gly Gly Asp Cys Ser Leu Asn Phe Asn Asp Pro Trp 1485 1480 Lys Asn Cys Thr Gln Ser Leu Gln Cys Trp Lys Tyr Phe Ser Asp Gly His Cys Asp Ser Gln Cys Asn Ser Ala Gly Cys Leu Phe Asp Gly Phe 1515 1510 Asp Cys Gln Arg Ala Glu Gly Gln Cys Asn Pro Leu Tyr Asp Gln Tyr 1530 Cys Lys Asp His Phe Ser Asp Gly His Cys Asp Gln Gly Cys Asn Ser 1545 Ala Glu Cys Glu Trp Asp Gly Leu Asp Cys Ala Glu His Val Pro Glu 1560 Arg Leu Ala Ala Gly Thr Leu Val Val Val Leu Met Pro Pro Glu 1575 Gln Leu Arg Asn Ser Ser Phe His Phe Leu Arg Glu Leu Ser Arg Val 1595 Leu His Thr Asn Val Val Phe Lys Arg Asp Ala His Gly Gln Gln Met Ile Phe Pro Tyr Tyr Gly Arg Glu Glu Glu Leu Arg Lys His Pro Ile 1630 1625 1620 Lys Arg Ala Ala Glu Gly Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln 1640 Val Lys Ala Ser Leu Leu Pro Gly Gly Ser Glu Gly Gly Arg Arg Arg Arg Glu Leu Asp Pro Met Asp Val Arg Gly Ser Ile Val Tyr Leu Glu 1675 1670 1665 Ile Asp Asn Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe Gln Ser 1695 1690 1685

WO 94/07474 PCT/US93/09338

Ala Thr Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser 1700 1705 1710

Leu Asn Ile Pro Tyr Lys Ile Glu Ala Val Gln Ser Glu Thr Val Glu 1715 1720 1725

Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala Ala Ala 1730 1740

Phe Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser Arg Lys 1745 1750 1755 1760

Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val 1765 1770 1775

Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Glu Leu Gly Glu Asp Ser 1780 1785 1790

Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp 1795 1800 1805

Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe 1810... 1815 1820

Arg Phe Glu Glu Pro Val Val Leu Pro Asp Leu Asp Asp Gln Thr Asp 1825 1830 1835 1840

His Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met 1845 1850 1855

Ser Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val Asp Ala Asp Cys 1860 1865 1870

Met Asp Val Asn Val Arg Gly Pro Asp Gly Phe Thr Pro Leu Met Ile 1875 1880 1885

Ala Ser Cys Ser Gly Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu 1890 1895 1900

Glu Asp Ala Pro Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser 1905 1910 1915 1920

Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His Leu Ala 1925 1930 1935

Ala Arg Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser 1940 1945 1950

Ala Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His Ala 1955 1960 1965

Ala Val Ser Ala Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn 1970 1975 1980

Arg Ala Thr Asp Leu Asp Ala Arg Met His Asp Gly Thr Thr Pro Leu 1985 1990 1995 2000

Ile Leu Ala Ala Arg Leu Ala Val Glu Gly Met Leu Glu Asp Leu Ile 2005 2010 2015

Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu Gly Lys Ser Ala 2020 2025 2030

Leu His Trp Ala Ala Ala Val Asn Asn Val Asp Ala Ala Val Leu 2035 2040 2045

Leu Lys Asn Gly Ala Asn Lys Asp Met Gln Asn Asn Arg Glu Glu Thr

-134-Pro Leu Phe Leu Ala Ala Arg Glu Gly Ser Tyr Glu Thr Ala Lys Val Leu Leu Asp His Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp Ile Ala Gln Glu Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu Tyr Asn Leu Val Arg Ser Pro Gln Leu His Gly Ala Pro Leu Gly Gly Thr Pro Thr Leu Ser Pro Pro Leu Cys Ser Pro Asn Gly Tyr Leu Gly Ser Leu Lys Pro Gly Val Gln Gly Lys Lys Val Arg Lys Pro Ser Ser Lys Gly Leu Ala Cys Gly Ser Lys Glu Ala Lys Asp Leu Lys Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys Leu Leu Asp Ser Ser Gly Met Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Leu Pro Ser Pro Phe Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro Gly Met Pro Asp Thr His Leu Gly Ile Gly His Leu Asn Val Ala Ala Lys Pro Glu Met Ala Ala Leu Gly Gly Gly Arg Leu Ala Phe Glu Thr Gly Pro Pro Arg Leu Ser His Leu Pro Val Ala Ser Gly Thr Ser Thr Val Leu Gly Ser Ser Ser Gly Gly Ala Leu Asn Phe Thr Val Gly Gly Ser Thr Ser Leu Asn Gly Gln Cys Glu Trp Leu Ser Arg Leu Gln Ser Gly Met Val Pro Asn Gln Tyr Asn Pro Leu Arg Gly Ser Val Ala Pro Gly Pro Leu Ser Thr Gln Ala Pro Ser Leu Gln His Gly Met Val Gly Pro Leu His Ser Ser Leu Ala Ala Ser Ala Leu Ser Gln Met Met Ser Tyr Gln Gly Leu Pro Ser Thr Arg Leu Ala Thr Gln Pro His Leu Val Gln Thr Gln Gln Val Gln Pro Gln Asn Leu Gln Met Gln Gln Gln Asn Leu Gln Pro

Ala Asn Ile Gln Gln Gln Ser Leu Gln Pro Pro Pro Pro Pro Pro

240

288

								-	135-								
	Gln	Pro	His	Leu 242	_	Val	Ser	Ser	Ala 242		Ser	Gly	His	Leu 2430		Arg	
	Ser	Phe	Leu 243		Gly	Glu	Pro	Ser 244		Ala	Asp	Val	Gln 2445		Leu	Gly	
	Pro	Ser 245	Ser	Leu	Ala	Val	His 245		Ile	Leu	Pro	Gln 2460		Ser	Pro	Ala	
	Leu 246		Thr	Ser	Leu	Pro 247		Ser	Leu	Val	Pro 247		Val	Thr	Ala	Ala 2480	
	Gln	Phe	Leu	Thr	Pro 248!		Ser	Gln	His	Ser 2490		Ser	Ser	Pro	Val 2495		
	Asn	Thr	Pro	Ser 2500		Gln	Leu	Gln	Val 2505		Glu	His	Pro	Phe 2510		Thr	
	Pro	Ser	Pro 2515		Ser	Pro	Asp	Gln 2520		Ser	Ser	Ser	Ser 2525		His	Ser	
	Asn	Val 2530	Ser)	Asp	Trp	Ser	Glu 2535	-	Val	Ser	Ser	Pro 2540		Thr	Ser	Met	
	Gln 2545		Gln	Ile		Arg 2550		Pro	Glu	Ala	Phe 2555						
(2)	INFO	ITAMS	ON F	OR S	EQ I	D NC	21:	:									
	(i)	(Ā) (B) (C)	ENCE LEN TYP STR TOP	GTH: E: II ANDE	972 ucle DNES	3 ba ic a s: d	ase p acid doubl	airs				-			-		
-	(ii)	MOLE	CULE	TYP	E: c	:DNA											
	(ix)	(A)	URE: NAM LOC	E/KE			419										
	(xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	21:			•				
GGA2	ATTCCG		Ala				_				_	Leu	_				48
CTC Leu	TGG C Trp L 15	TG T eu C	GC T	GC G	la A	CC C la P 20	CC G	CG C	AT G is A	la L	TG C eu G 25	AG T ln C	GT C ys A	GA G rg A	AT sp		96
	TAT G Tyr G			ys V					et C					is A			144

GGC ACA GGA TAC TGC AAA TGT CCA GAA GGC TTC TTG GGG GAA TAT TGT

CAA CAT CGA GAC CCC TGT GAG AAG AAC CGC TGC CAG AAT GGT GGG ACT

Gln His Arg Asp Pro Cys Glu Lys Asn Arg Cys Gln Asn Gly Gly Thr

TGT GTG GCC CAG GCC ATG CTG GGG AAA GCC ACG TGC CGA TGT GCC TCA Cys Val Ala Gln Ala Met Leu Gly Lys Ala Thr Cys Arg Cys Ala Ser

50

Gly Thr Gly Tyr Cys Lys Cys Pro Glu Gly Phe Leu Gly Glu Tyr Cys .

	⁻ 80			85					90					-
GGG TTT Gly Phe 95	ACA GGA Thr Gly	GAG GAG Glu As	C TGC Cys 100	CAG Gln	TAC Tyr	TCA Ser	ACA Thr	TCT Ser 105	CAT His	CCA Pro	TGC	TTT Phe		336
GTG TCT Val Ser 110	CGA CCC Arg Pro	TGC CTC Cys Let 11!	ı Asn	GGC Gly	GGC Gly	ACA Thr	TGC Cys 120	CAT	ATG Met	CTC Leu	AGC Ser	CGG Arg 125		384
GAT ACC Asp Thr	TAT GAG Tyr Glu	TGC ACC	Cys	CAA Gln	GTC Val	GGG Gly 135	TTT Phe	ACA Thr	GGT Gly	AAG Lys	GAG Glu 140	Cys		432
CAA TGG Gln Trp	ACG GAT Thr Asp 145	Ala Cy	C CTG Leu	TCT Ser	CAT His 150	CCC Pro	TGT Cys	GCA Ala	Asn	GGA Gly 155	AGT Ser	ACC Thr		480
TGT ACC Cys Thr	ACT GTG Thr Val 160	GCC AAG Ala Ası	CAG Gln	TTC Phe 165	TCC Ser	TGC Cys	AAA Lys	TGC Cys	CTC Leu 170	ACA Thr	GGC	TTC Phe		528
ACA GGG Thr Gly 175	CAG AAA Gln Lys	TGT GAO	ACT Thr 180	Asp	GTC Val	AAT Asn	GAG Glu	TGT Cys 185	GAC Asp	ATT	CCA Pro	GGA Gly		576
CAC TGC His Cys 190	CAG CAT Gln His	GGT GGG Gly Gly 195	Thr	TGC Cys	CTC Leu	AAC Asn	CTG Leu 200	CCT Pro	GGT Gly	TCC Ser	TAC Tyr	CAG Gln 205		624
TGC CAG Cys Gln	TGC CCT Cys Pro	CAG GGG Gln Gly 210	TTC Phe	ACA Thr	GGC	CAG Gln 215	TAC Tyr	TGT Cys	GAC Asp	AGC Ser	CTG Leu 220	TAT Tyr	·	672
GTG CCC Val Pro	TGT GCA Cys Ala 225	CCC TCP Pro Ser	CCT Pro	TGT Cys	GTC Val 230	AAT Asn	GGA Gly	GGC Gly	ACC Thr	TGT Cys 235	CGG Arg	CAG Gln		720
ACT GGT (GAC TTC Asp Phe 240	ACT TTT Thr Phe	GAG Glu	TGC Cys 245	AAC Asn	TGC Cys	CTT Leu	CCA Pro	GGT Gly 250	TTT Phe	GAA Glu	GGG Gly		768
AGC ACC Ser Thr (255	TGT GAG Cys Glu	AGG AAT	ATT Ile 260	GAT Asp	GAC Asp	TGC Cys	CCT Pro	AAC Asn 265	CAC His	AGG Arg	TGT Cys	CAG Gln		816
AAT GGA (Asn Gly (270	GGG GTT Gly Val	TGT GTG Cys Val 275	Asp	GGG Gly	GTC Val	AAC Asn	ACT Thr 280	TAC Tyr	AAC Asn	TGC Cys	CGC Arg	TGT Cys 285		864
CCC CCA (CAA TGG Gln Trp	ACA GGA Thr Gly 290	CAG Gln	TTC Phe	TGC Cys	ACA Thr 295	GAG Glu	GAT Asp	GTG Val	GAT Asp	GAA Glu 300	TGC Cys		912
CTG CTG (Leu Leu (CAG CCC Sln Pro 305	AAT GCC Asn Ala	TGT Cys	Gln	AAT Asn 310	GGG Gly	GGC Gly	ACC Thr	TGT Cys	GCC Ala 315	AAC Asn	CGC Arg		960
AAT GGA G Asn Gly G	GGC TAT Gly Tyr G20	GGC TGT Gly Cys	Val	TGT Cys 325	GTC Val	AAC Asn	GJA GGC	TGG Trp	AGT Ser 330	GGA Gly	GAT Asp	GAC Asp	1	800
TGC AGT C Cys Ser C 335	GAG AAC Glu Asn	ATT GAT Ile Asp	GAT Asp 340	TGT Cys	GCC Ala	TTC Phe	Ala	TCC Ser 345	TGT Cys	ACT Thr	CCA Pro	GLY	1	056
TCC ACC T	GC ATC	GAC CGT	GTG (GCC	TCC	TTC	TCT	TGC	ATG	TGC	CCA	GAG	1	104

Ser 350		Cys	Ile	Asp	Arg 355		Ala	Ser	Phe	Ser 360		Met	Cys	Pro	Glu 365		
GGG	AAG Lys	GCA Ala	GGT Gly	CTC Leu 370	Leu	TGT	CAT His	CTG Leu	GAT Asp 375	GAT Asp	GCA Ala	TGC Cys	ATC	AGC Ser 380	AAT Asn	1:	152
				Gly					Thr					Gly	CAA Gln	1:	200
			Thr										Cys		GAA Glu	1:	248
		Asp													GCA Ala	1:	296
	Lys														AAG Lys 445	1:	344
														CAT His 460	TCA Ser	13	392
														GGC	TTC Phe	14	440
														TTA Leu	GAA Glu	. 14	488
														TGT Cys		15	536
														ACT Thr	GGG Gly 525	15	584
														TGT Cys 540		ļé	532
														CAG Gln		1 <i>6</i>	580
GCC Ala	ACA Thr	GGT Gly 560	TTC Phe	ACT Thr	GGT Gly	GTG Val	TTG Leu 565	TGT Cys	GAG Glu	GAG Glu	AAC Asn	ATT Ile 570	GAC Asp	AAC Asn	TGT Cys	17	728
														GAT Asp		17	776
TAC Tyr 590	ACC Thr	TGC Cys	ATC Ile	TGC Cys	AAT Asn 595	CCC Pro	Gly	TAC Tyr	ATG Met	GGC Gly 600	GCC Ala	ATC Ile	TGC Cys	AGT Ser	GAC Asp 605	18	324
CAG Gln	ATT Ile	GAT Asp	GAA Glu	TGT Cys 610	TAC Tyr	AGC Ser	AGC Ser	CCT Pro	TGC Cys 615	CTG Leu	AAC Asn	GAT Asp	GGT Gly	CGC Arg 620	TGC Cys	18	372

-138-

				l As					s Ası					y Th	G TCA r Ser	1920
			n Cy					As _I					As		T TGT o Cys	1968
		s Gl					Gly					Sex			C TGC 1 Cys	2016
	r Pr					/ Gln					Asp				G TGT u Cys 685	2064
					a Arc					Cys					G AAT l Asn O	2112
				s Ile					Pro					Cys	TAC Tyr	2160
			l As										Gly		Cys	2208
AC1 Thr	GG! Gly 735	/ Gly	r cro y Let	C AGI	GGA Gly	TAT Tyr 740	AAG Lys	TGT Cys	CTC Leu	TGT Cys	GAT Asp 745	GCA Ala	GGC	TGG	GTT Val	2256
GGC Gly 750	, Ile	AAC Ası	TG1	GAA Glu	GTG Val 755	GAC Asp	AAA Lys	AAT Asn	GAA Glu	TGC Cys 760	CTT Leu	TCG Ser	AAT Asn	CCA Pro	TGC Cys 765	2304
CAG Gln	AAT Asn	GGA Gly	GGA Gly	ACT Thr 770	Cys	GAC	AAT Asn	CTG Leu	GTG Val 775	AAT Asn	GGA Gly	TAC Tyr	AGG Arg	TGT Cys 780	Thr	2352
TGC Cys	AAG Lys	Lys	GGC Gly 785	Phe	AAA Lys	GGC Gly	TAT Tyr	AAC Asn 790	TGC Cys	CAG Gln	GTG Val	AAT Asn	ATT Ile 795	GAT Asp	GAA Glu	2400
TGT Cys	GCC	TCA Ser 800	Asn	CCA Pro	TGC Cys	CTG Leu	AAC Asn 805	CAA Gln	GGA Gly	ACC Thr	TGC Cys	TTT Phe 810	GAT Asp	GAC Asp	ATA Ile	2448
AGT Ser	GGC Gly 815	TAC Tyr	ACT Thr	TGC Cys	CAC	TGT Cys 820	GTG Val	CTG Leu	CCA Pro	TAC Tyr	ACA Thr 825	GGC Gly	AAG Lys	AAT Asn	TGT Cys	2496
CAG Gln 830	ACA Thr	GTA Val	TTG Leu	GCT Ala	CCC Pro 835	TGT Cys	TCC Ser	CCA Pro	AAC Asn	CCT Pro 840	TGT Cys	GAG Glu	AAT Asn	GCT Ala	GCT Ala 845	2544
GTT Val	TGC Cys	AAA Lys	GAG Glu	TCA Ser 850	CCA Pro	AAT Asn	TTT Phe	GAG Glu	AGT Ser 855	TAT Tyr	ACT Thr	TGC Cys	TTG Leu	TGT Cys 860	GCT Ala	2592
CCT Pro	GGC Gly	TGG Trp	CAA Gln 865	GGT Gly	CAG Gln	CGG (Arg (Cys	ACC Thr 870	ATT Ile	GAC . Asp	ATT Ile	GAC Asp	GAG Glu 875	TGT Cys	ATC Ile	2640
						CAT (Asn					2688 .

TAC ATG TOT GAA TOT CCA CCA GGG TTC ACT GGT ATG GAC TOT GAG GAG TYP Met Cys Glu Cys Pro Pro Gly Phe Ser Gly Met Asp Cys Glu Glu 905 GAC ATT GAT GAC TGC CTT GCC AAT CCT TGC CAG AAT GGA GGT TCC TGT APP ILE ASP ASP Cys Leu Ala Asn Pro Cys Gln Asn GGA GGT TCC TGT APP ILE ASP ASP Cys Leu Ala Asn Pro Cys Gln Asn Gly Gly Ser Cys 910 ATG GAT GGA GTG AAT ACT TTC TCC TGC CTT TCC CTT CCC GGT TTC ACT MET ASP Gly Val Asn Thr Phe Ser Cys Leu Cys Leu Pro Gly Phe Thr 930 GGG GAT AAG TGC CAG ACA GAC ATG AAT GAG TGT CTC AGT GAA CCC TGT GGLY ASP Lys Cys Gln Thr Asp Met Asn Glu Cys Leu Ser Glu Pro Cys 945 AAG AAT GGA GGG ACC TGC TCT GAC TAC GTC AAC AGT TAC ACT TGC AAG Lys Asn Gly Gly Thr Cys Ser Asp Tyr Val Asn Ser Tyr Thr Cys Lys 965 TCC CAG GCA GGA TTT GAT GGA GTC CAT TGT GAG AAC ACT AAT GAG Cys Gln Ala Gly Phe Asp Gly Val His Cys Glu Asn Asn Ile Asn Glu 975 TCC CAC GAG AGA TTT GAT GGA GTC CAT TGT GAG AAC AAC ATC AAT GAG Cys Gln Ala Gly Phe Asp Gly Val His Cys Glu Asn Asn Ile Asn Glu 995 TCC ACT GAG AGC TCC TCT TTC AAT GGT GGC ACA TGT GTT GAT GGG ATT Cys Thr Glu Ser Ser Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile 990 AAC TCC TCT TGC TTG TGC CCT GTG GGT TTC ACT GGT TCC TCT TGC TGC CYS Phe Asn Glu Cys Pro Val Gly Phe Thr Gly Ser Phe Cys 1010 CTC CAT GAG AAT AAT GAA TGC AGC TCT TTC ACT GCT TGC TACT GAG GGA TCC TTT TGC TGC CCT GTG GGT TTC ACT GCA TCC TCC TGC CAT GAG AAT AAT GAA TGC AGC TCT GAT CCA TGC CCC CTG GGC AAC TGT GAT GGC CTG GGT ACC TAC CCC TGC GAC TGC CCC TG GGC TAC GGG AAA AAC TGT CAC TGC TGC TTC TACT TGC TGC CAT GAG AAT AAT GAA TGC AGC TCC TGT TCA CCA TGC CCC CTG GGC TACT GAG GAA TAC AAT GAA TGC AGC TCC TGC TGC TCC CAT GAG AAA AAC TGT CAC TGC TGC AGC TGC CCC CTG GGC TACT GAT GAT GAA CAC TTC TGT TGT CAC TGC TGC TGC TGC TGC TACT GAT GAC CTC TGC GGT ACC TCC TGC AGC TGC CCC TGC GGC TACT TGT GAT GGC CTC GGT ACC TGC TGC AGC TGC CCC TGC GGC TACT TGT GAT GGC CTC GGT ACC TGC TGC AGC TGC CCC TGC GGC TACT TGT GAT GGC CTC TGC ACC CTC GGC GGC CAA AAA AAC GGT TCC CCC TGC CAT TGT CAC ATA ACT GGC GGT GGT CTT TGT GAG CAC CTC TGT																		
App Tie Asp Asp Cys Leu Ala Asp Pro Cys Gin Asp Gly Ser Cys 915 915 925	TAC	Met	Cys	GAA Glu	TG1 Cys	CCA Pro	Pro	Gly	TTC Phe	AGT Ser	GGI	Met	Asp	TGT Cys	GAG Glu	GAG Glu	27:	36
Met Asp Gly Val Asn Thr Phe Ser Cys Leu Cys Leu Pro Gly Phe Thr 940 930 930 231 232 232 232 232 232 232 232 233 <td>Asp</td> <td>Ile</td> <td></td> <td></td> <td></td> <td>Leu</td> <td>Ala</td> <td></td> <td></td> <td></td> <td>Gln</td> <td>Asn</td> <td></td> <td></td> <td></td> <td>Cys</td> <td>278</td> <td>34</td>	Asp	Ile				Leu	Ala				Gln	Asn				Cys	278	34
Gly Asp Lys Cys Gln Thr Asp Met Asn Glu Cys Leu Ser Glu Pro Cys 945 945 955 955 955 955 955 955 955 955	ATG Met	GAT	GGA Gly	GTG Val	Asn	Thr	TTC Phe	TCC Ser	TGC Cys	Leu	Cys	CTT Leu	CCG Pro	GGT Gly	Phe	Thr	283	32
Topic Ash Cly Cly Thr Cys Ser Ash Tyr Val Ash Ser Tyr Thr Cys Lys 960 965 965 965 965 965 965 970 965 970 965 970 965 970 965 970 975 97	GGG Gly	GAT Asp	AAG Lys	Сув	Gln	ACA Thr	GAC Asp	ATG Met	Asn	GAG Glu	TGT Cys	CTG Leu	AGT Ser	Glu	CCC Pro	TGT	288	30
Cys Gln Ala Cly Phe Asp Cly Val His Cys Glu Asn Asn Ile Asn Glu 975 985 980 980 385 385 3024 <td></td> <td></td> <td>Gly</td> <td>Gly</td> <td></td> <td></td> <td></td> <td>Asp</td> <td>Tyr</td> <td></td> <td></td> <td></td> <td>Tyr</td> <td></td> <td></td> <td></td> <td>292</td> <td>28</td>			Gly	Gly				Asp	Tyr				Tyr				292	28
Cys Thr Glu Ser Ser Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile 995 AAC TCC TTC TCT TGC TTG TGC CCT GTG GGT TTC ACT GGA TCC TTC TGC Asn Ser Phe Ser Cys Leu Cys Pro Val Gly Phe Thr Gly Ser Phe Cys 1010 CTC CAT GAG ATC AAT GAA TGC AGC TCT CAT CCA TGC CTG AAT GAG GGA Leu His Glu Ile Asn Glu Cys Ser Ser His Pro Cys Leu Asn Glu Gly 1025 ACG TGT GTT GAT GGC CTG GGT ACC TAC CGC TGC AGC TGC CTG GGC Thr Cys Val Asp Gly Leu Gly Thr Tyr Arg Cys Ser Cys Pro Leu Gly 1040 TAC ACT GGG AAA AAC TGT CAA ACC CTG GTG AAT CTC TGC AGT GGC TYr Thr Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser Arg Ser 1055 CCA TGT AAA AAC AAA GGT ACT TGT GTT CAG AAA AAA GCA GAG TCC CAG PTC Cys Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln 1070 TGC CTA TGT CCA TCT GGA TGG GCT GGT GCC TAT TGT GAC GTG CCC AAT Cys Leu Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn 1090 GTC TCT TGT GAC ATA GCA GCC TCC AGG AGA GGT CTG CTG GTG CTG Val Ser Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His 1105 TTG TGC CAG CAC TCA GGT GTC TGC AGT CAT TGT GAC GAC CAT TAC Val Ser Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His 1105 TTG TGC CAG CAC TCA GGT GTC TGC ATC AAT GCT GGC AAC CAC CAT TAC Cys Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr 1120 TGT CAG TGC CCC CTG GGC TAT ACT GGG AGC TAC TGT GAC GAC CAT TAC Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Glu Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAC CAC GGG GCA ACA CAC ACG Asp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp	TGC Cys	Gln	Ala	GGA Gly	TTT Phe	GAT Asp	Gly	GTC Val	CAT His	TGT	GAG Glu	Asn	AAC Asn	ATC Ile	AAT Asn	GAG Glu	297	16
Asn Ser Phe Ser Cys Leu Cys Pro Val Gly Phe Thr Gly Ser Phe Cys 1010 CTC CAT GAG ATC AAT GAA TGC AGC TCT CAT CCA TCC CTG AAT GAG GGA Leu His Glu Ile Asn Glu Cys Ser Ser His Pro Cys Leu Asn Glu Gly 1025 ACG TGT GTT GAT GGC CTG GGT ACC TAC CGC TGC AGC TGC CCC CTG GGC 3168 Thr Cys Val Asp Gly Leu Gly Thr Tyr Arg Cys Ser Cys Pro Leu Gly 1040 TAC ACT GGG AAA AAC TGT CAG ACC CTG GTG AAT CTC TGC AGT CGG TCT GTY Thr Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser Arg Ser 1055 CCA TGT AAA AAC AAA GGT ACT TGT GTT CAG AAA CC CAG AAA AAA GCA GAG TCC CAG Fro Cys Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln 1075 TGC CTA TGT CCA TCT GGA TGG GCT GGT GCT TAT TGT GAC GTG CCC AAT Cys Leu Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn 1090 GTC TCT TGT GAC ATA GCA GCC TCC AGG AGA GGT GTG CTT GTA GAA CAC CAT TGT GTA Arg Arg Arg Gly Val Leu Val Glu His 1105 TTG CAG CAC TCA GGT GTC TGC ATC AAT GCT GGC AAC ACG CAT TAC CAG CYs Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His Tyr 1120 GTC TAG TGC CAC CCC CTG GGC TAT ACT GGG AGC TAC TGT GAC GAG CAA CAC CAT TAC CYS Gln Cys Pro Leu Gly Tyr Thr Glys Ir Tyr Cys Glu Glu Glu Gln Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GAG GGA ACA TGC AGT GAC ASp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp	Cys					Cys					Thr	Cys				Ile	302	24
Leu His Glu Ile Asn Glu Cys Ser Ser His Pro Cys Leu Asn Glu Gly 1035 ACG TGT GTT GAT GGC CTG GGT ACC TAC CGC TGC AGC TGC CCC CTG GGC 3168 Thr Cys Val Asp Gly Leu Gly Thr Tyr Arg Cys Ser Cys Pro Leu Gly 1040 TAC ACT GGG AAA AAC TGT CAG ACC CTG GTG AAT CTC TGC AGT CGG TCT 3216 TYr Thr Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser Arg Ser 1055 CCA TGT AAA AAC AAA GGT ACT TGT GTT CAG AAA AAA GCA GAG TCC CAG Pro Cys Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln 1070 TGC CTA TGT CCA TCT GGA TGG GCT GGT GCC TAT TGT GAC CTA TGT CAG ASN 1085 TGC CTA TGT GAC ATA GCA GCC TCC AGG AGA GGT GCC CAAT 10090 GTC TCT TGT GAC ATA GCA GCC TCC AGG AGA GGT GTG CCC AAT 1000 GTC TCT TGT GAC ATA GCA GCC TCC AGG AGA GGT GTG CTT GAA CAC Val Ser Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His 1110 TTG TGC CAG CAC TCA GGT GTC TGC ATC AAT GCT GGC AAC ACG CAT TAC AST 1120 TCT CAG TGC CCC CTG GGC TAT ACT GGG ACC TAC TAC TGT GAG GAG GAG CAA CTC Cys Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr 1120 TCT CAG TGC CCC CTG GGC TAT ACT GGG ACC TAC TAC TGT GAG GAG CAA CTC Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Glu Gln Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GGG GCA ACA TGC AGT GAC ASp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp					Сув	Leu				Gly	Phe				Phe	Cys	.307	'2
Thr Cys Val Asp Gly Leu Gly Thr Tyr Arg Cys Ser Cys Pro Leu Gly 1040 TAC ACT GGG AAA AAC TGT CAG ACC CTG GTG AAT CTC TGC AGT CGG TCT TYr Thr Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser Arg Ser 1055 CCA TGT AAA AAC AAA GGT ACT TGT GTT CAG AAA AAA GCA GAG TCC CAG Pro Cys Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln 1070 TGC CTA TGT CCA TCT GGA TGG GCT GGT GCC TAT TGT GAC GAC GAC GAC CCC AAT Cys Leu Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn 1090 GTC TCT TGT GAC ATA GCA GCC TCC AGG AGA GGT GTG CTT GTT GAA CAC Val Ser Cys Asp 1le Ala Ala Ser Arg Arg Gly Val Leu Val Glu His 1115 TTG TGC CAG CAC TCA GGT GTC TGC ATC AAT GCT GGC AAC ACC CAT TAC Cys Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr 1120 TGT CAG TGC CCC CTG GGC TAT ACT GGG AGC TAC TGT GAG GAG CAA CTC Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Glu Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GGG GCA ACA TGC AGT GAC ASp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp				Ile	Asn				Ser	His				Asn	Glu		312	:O
Tyr Thr Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser Arg Ser 1055 CCA TGT AAA AAC AAA GGT ACT TGT GTT CAG AAA AAA GCA GAG TCC CAG Pro Cys Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln 1070 TGC CTA TGT CCA TCT GGA TGG GCT GGT GCC TAT TGT GAC GTG CCC AAT Cys Leu Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn 1090 GTC TCT TGT GAC ATA GCA GCC TCC AGG AGA GGT GTG CTT GTT GAA CAC Val Ser Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His 1115 TTG TGC CAG CAC TCA GGT GTC TGC ATC AAT GCT GGC AAC ACG CAT TAC Leu Cys Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr 1120 TGT CAG TGC CCC CTG GGC TAT ACT GGG AGC TAC TGT GAG GAG CAA CTC Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Gln Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GGG GCA ACA TGC AGT GAC ASp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp			Val	Asp				Thr	Tyr				Cys	Pro			316	.8
Pro Cys Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln 1070 TGC CTA TGT CCA TCT GGA TGG GCT GGT GCC TAT TGT GAC GTG CCC AAT Cys Leu Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn 1090 GTC TCT TGT GAC ATA GCA GCC TCC AGG AGA GGT GTG CTT GTT GAA CAC Val Ser Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His 1105 TTG TGC CAG CAC TCA GGT GTC TGC ATC AAT GCT GGC AAC ACG CAT TAC Leu Cys Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr 1120 TGT CAG TGC CCC CTG GGC TAT ACT GGG AGC TAC TGT GAG GAG CAA CTC Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Gln Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GGG GCA ACA TGC AGT GAC Asp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp		Thr	Gly				Gln	Thr				Leu	Cys				321	6
Cys Leu Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn 1090 GTC TCT TGT GAC ATA GCA GCC TCC AGG AGA GGT GTG CTT GTT GAA CAC Val Ser Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His 1105 TTG TGC CAG CAC TCA GGT GTC TGC ATC AAT GCT GGC AAC ACG CAT TAC Leu Cys Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr 1120 TGT CAG TGC CCC CTG GGC TAT ACT GGG AGC TAC TGT GAG GAG CAA CTC Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Glu Gln Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GGG GCA ACA TGC AGT GAC ASp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp	Pro	Cys				Gly	Thr				Lys	Lys				Gln	326	4
Val Ser Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His 1105 TTG TGC CAG CAC TCA GGT GTC TGC ATC AAT GCT GGC AAC ACG CAT TAC Leu Cys Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr 1120 TGT CAG TGC CCC CTG GGC TAT ACT GGG AGC TAC TGT GAG GAG CAA CTC Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Gln Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GGG GCA ACA TGC AGT GAC Asp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp					Ser	Gly				Ala	Tyr				Pro	Asn	331	2
Leu Cys Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr 1120 TGT CAG TGC CCC CTG GGC TAT ACT GGG AGC TAC TGT GAG GAG CAA CTC Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Gln Leu 1135 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GGG GCA ACA TGC AGT GAC Asp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp				Asp	Ile				Arg	Arg				Val	Glu			0
Cys Gln Cys Pro Leu Gly Tyr Thr Gly S r Tyr Cys Glu Glu Gln Leu 1135 1140 1145 GAT GAG TGT GCG TCC AAC CCC TGC CAG CAC GGG GCA ACA TGC AGT GAC Asp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp	TTG Leu	TGC Cys	Gln	His	TCA Ser	GGT Gly	GTC Val	Cys	Ile	AAT Asn	GCT Ala	GGC	Asn	Thr	CAT His	TAC Tyr	340	8
Asp Glu Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp		Gln	Cys				Tyr	Thr				Cys	Glu				345	6
	Asp	Glu	TGT Cys	GCG Ala	TCC Ser	Asn	Pro	TGC Cys	CAG Gln	CAC His	Gly	Ala	ACA Thr	TGC Cys	AGT Ser	Asp	350	4

TTC Phe	ATT	Gly	GGA Gly	TAC Tyr 117	Arg	TGC Cys	GAG Glu	TGT Cys	GTC Val 117	Pro	GGC Gly	TAT Tyr	CAG Gln	GGT Gly 118	val	3552
AAC Asn	TGT Cys	GAG Glu	TAT Tyr 118	Glu	GTG Val	GAT Asp	GAG Glu	TGC Cys 119	Gln	AAT Asn	CAG Gln	CCC Pro	TGC Cys 119	Gln	AAT Asn	3600
GGA Gly	GGC Gly	ACC Thr 120	Cys	ATT Ile	GAC Asp	CTT Leu	GTG Val 120	Asn	CAT His	TTC Phe	AAG Lys	TGC Cys 121	Ser	TGC Cys	CCA Pro	3648
CCA Pro	GGC Gly 121	Thr	CGG Arg	GGC Gly	CTA Leu	CTC Leu 122	Cys	GAA Glu	GAG Glu	AAC Asn	ATT Ile 122	Asp	GAC Asp	Cys	GCC Ala	3696
CGG Arg 123	GGT Gly O	CCC Pro	CAT His	TGC Cys	CTT Leu 123	Asn	GGT Gly	GGT Gly	CAG Gln	TGC Cys 1240	Met	GAT Asp	AGG Arg	ATT Ile	GGA Gly 1245	3744
GGC Gly	TAC Tyr	AGT Ser	TGT Cys	CGC Arg 1250	Cys	TTG Leu	CCT Pro	GGC	TTT Phe 125	Ala	GGG Gly	GAG Glu	CGT Arg	TGT Cys 126	Glu	3792
GGA Gly	GAC Asp	ATC Ile	AAC Asn 126	Glu	TGC Cys	CTC Leu	TCC Ser	AAC Asn 127	Pro	TGC Cys	AGC Ser	TCT Ser	GAG Glu 127	Gly	AGC Ser	3840
CTG Leu	GAC Asp	TGT Cys 128	Ile	CAG Gln	CTC Leu	ACC Thr	AAT Asn 128	Asp	TAC Tyr	CTG Leu	TGT Cys	GTT Val 1290	Cys	CGT Arg	AGT Ser	3888
GCC Ala	TTT Phe 1295	Thr	GGC Gly	CGG Arg	CAC His	TGT Cys 1300	Glu	ACC Thr	TTC Phe	GTC Val	GAT Asp 130	Val	TGT Cys	ccc Pro	CAG Gln	3936
ATG Met 1319	CCC Pro	TGC Cys	CTG Leu	AAT Asn	GGA Gly 1315	Gly	ACT Thr	TGT Cys	GCT Ala	GTG Val 1320	Ala	AGT Ser	AAC Asn	ATG Met	CCT Pro 1325	3984
GAT Asp	GGT Gly	TTC Phe	ATT Ile	TGC Cys 1330	Arg	TGT Cys	CCC Pro	CCG Pro	GGA Gly 1335	Phe	TCC Ser	GGG Gly	GCA Ala	AGG Arg 1340	Cys	4032
CAG Gln	AGC Ser	AGC Ser	TGT Cys 1345	Gly	CAA Gln	GTG Val	AAA Lys	TGT Cys 1350	Arg	AAG Lys	GGG Gly	GAG Glu	CAG Gln 1355	Cys	GTG Val	4080
CAC His	ACC Thr	GCC Ala 1360	Ser	GGA Gly	CCC Pro	CGC Arg	TGC Cys 1365	Phe	TGC Cys	CCC Pro	AGT Ser	CCC Pro 1370	Arg	GAC Asp	TGC Cys	4128
GAG Glu	TCA Ser 1375	Gly	TGT Cys	GCC Ala	AGT Ser	AGC Ser 1380	Pro	TGC Cys	CAG Gln	CAC His	GGG Gly 1385	Gly	AGC Ser	TGC Cys	CAC His	4176
CCT Pro 1390	CAG Gln	CGC Arg	CAG Gln	CCT Pro	CCT Pro 1395	Tyr	TAC Tyr	TCC Ser	TGC Cys	CAG Gln 1400	Cys	GCC Ala	CCA Pro	CCA Pro	TTC Phe 1405	4224
TCG Ser	GGT Gly	AGC Ser	CGC Arg	TGT Cys 1410	Glu	CTC Leu	TAC Tyr	ACG Thr	GCA Ala 1415	Pro	CCC Pro	AGC Ser	ACC Thr	CCT Pro 1420	Pro	4272
GCC Ala	ACC Thr	Cys	CTG Leu 1425	Ser	CAG Gln	TAT Tyr	TGT Cys	GCC Ala 1430	Asp	AAA Lys	GCT Ala	CGG Arg	GAT Asp 1435	Gly	GTC Val	4320

ŤGT Cys	GAT Asp	GAG Glu 144	Ala	TGC Cys	AAC Asn	AGC Ser	CAT His 144	Ala	TGC Cys	CAG Gln	TGG Trp	GAT Asp 1450	GTA	GGT Gly	GAC Asp	43	68
TGT Cys	TCT Ser 145	Leu	ACC Thr	ATG Met	GAG Glu	AAC Asn 146	Pro	TGG Trp	GCC Ala	AAC Asn	TGC Cys 146	Ser	TCC Ser	CCA Pro	CTT Leu	44	16
CCC Pro 147	Cys	TGG Trp	GAT Asp	TAT Tyr	ATC Ile 147		AAC Asn	CAG Gln	TGT Cys	GAT Asp 148	Glu	CTG Leu	TGC Cys	AAC Asn	ACG Thr 1485	44	64
GTC Val	GAG Glu	TGC Cys	CTG Leu	TTT Phe 149	Asp	AAC Asn	TTT Phe	GAA Glu	TGC Cys 149	Gln	GGG Gly	AAC Asn	AGC Ser	AAG Lys 1500	Thr	45	12
TGC Cys	AAG Lys	TAT Tyr	GAC Asp 150	Lys	TAC Tyr	TGT Cys	GCA Ala	GAC Asp 151	His	TTC Phe	AAA Lys	GAC Asp	AAC Asn 151	His	TGT Cys	45	60
AAC Asn	CAG Gln	GGG Gly 152	Cys	AAC Asn	AGT Ser	GAG Glu	GAG Glu 152	Cys	GGT Gly	TGG Trp	GAT Asp	GGG Gly 1530	Leu	GAC Asp	TGT Cys	46	80
GCT Ala	GCT Ala 153	Asp	CAA Gln	CCT Pro	GAG Glu	AAC Asn 1540	Leu	GCA Ala	GAA Glu	GGT Gly	ACC Thr 1545	Leu	GTT Val	ATT Ile	GTG Val	46	56
GTA Val 155	Leu	ATG Met	CCA Pro	CCT	GAA Glu 155	CAA Gln	CTG Leu	CTC Leu	CAG Gln	GAT Asp 1560	Ala	CGC Arg	AGC Ser	TTC Phe	TTG Leu 1565	47	04
CGG Arg	GCA Ala	CTG Leu	GGT Gly	ACC Thr 1570	Leu	CTC Leu	CAC His	ACC Thr	AAC Asn 1575	Leu	CGC Arg	ATT Ile	AAG Lys	CGG Arg 1580	Asp	47	52
TCC Ser	CAG Gln	G17 GGG	GAA Glu 158	Leu	ATG Met	GTG Val	TAC Tyr	CCC Pro 1590	Tyr	TAT Tyr	GGT Gly	GAG Glu	AAG Lys 1599	Ser	GCT Ala	48	00
GCT Ala	ATG Met	AAG Lys 1600	Lys	CAG Gln	AGG Arg	ATG Met	ACA Thr 160	Arg	AGA Arg	TCC Ser	CTT Leu	CCT Pro 1610	Gly	GAA Glu	CAA Gln	48	48
GAA Glu	CAG Gln 161	Glu	GTG Val	GCT Ala	GGC Gly	TCT Ser 1620	Lys	GTC Val	TTT Phe	CTG Leu	GAA Glu 1625	Ile	GAC Asp	AAC Asn	CGC Arg	48	96
CAG Gln 1630	Cys	GTT Val	CAA Gln	GAC Asp	TCA Ser 163	GAC Asp	CAC His	TGC Cys	TTC Phe	AAG Lys 1640	Asn	ACG Thr	GAT Asp	GCA Ala	GCA Ala 1645	49	44
GCA Ala	GCT Ala	CTC Leu	CTG Leu	GCC Ala 1650	Ser	CAC His	GCC Ala	ATA Ile	CAG Gln 1655	Gly	ACC Thr	CTG Leu	TCA Ser	TAC Tyr 1660	Pro	49	92
CTT Leu	GTG Val	TCT Ser	GTC Val 1669	Val	AGT Ser	GAA Glu	TCC Ser	CTG Leu 1670	Thr	CCA Pro	GAA Glu	CGC Arg	ACT Thr 1675	Gln	CTC Leu	50	40
CTC	TAT Tyr	CTC Leu 1680	Leu	GCT Ala	GTT Val	GCT Ala	GTT Val 1685	Val	ATC Ile	ATT Ile	CTG Leu	TTT Phe 1690	Ile	ATT Ile	CTG Leu	50	88
CTG Leu	GGG Gly 1695	Val	ATC Ile	ATG Met	GCA Ala	AAA Lys 1700	Arg	AAG Lys	CGT Arg	AAG Lys	CAT His 1705	Gly	TCT Ser	CTC Leu	TGG Trp	51.	36

	u Pr				ne Th						a Se				G CGT s Arg 172	
CG!	T GA g Gl	G CC u Pi	CA G' CO Va	al Gl	A CA y Gl '30	G GA n As	T GC	T GTO	G GGG 1 Gly 17	y Let	G AAI u Ly:	A AA' s Asi	r CT n Le	u Se	A GTG r Val 40	5232
			er G						y Thi					u Hi	C TGG s Trp	5280
		p As						Lys					Gl		T GAG p Glu	5328
GCC Ala	TT. Le	u Le	C TC u Se	A GA er Gl	A GA u Gl	A GA: u Asj 178	Asp	CCC Pro	ATI Ile	GAT Asp	CGA Arg 178	Arc	CC Pro	A TG	G ACA p Thr	5376
CAG Gln 179	Gl	G CA n Hi	C CI	T GA	A GC: u Ala 179	a Ala	A GAC	ATC Ile	C CGI	AGG Arg 180	Thr	CCA Pro	TCO Ser	CTC	G GCT 1 Ala 1805	5424
CTC Leu	ACC Thi	C CC	T CC o Pr	T CA O Gl: 18	n Ala	A GAG a Glu	G CAG	GAG Glu	GTG Val 181	Asp	GTG Val	TTA Leu	GAT Asp	GTG Val 182	G AAT L Asn 20	5472
GTC Val	Arg	r GG J Gl	c cc y Pr 18	o Asj	r GG(C TGC	ACC Thr	CCA Pro 183	Leu	ATG Met	TTG Leu	GCT Ala	TCI Ser 183	Let	C CGA Arg	5520
GGA Gly	GGC	Se:	r Se	A GAT	r TTG Leu	AGT Ser	GAT Asp 184	Glu	GAT Asp	GAA Glu	GAT Asp	GCA Ala 185	Glu	GAC Asp	TCT Ser	5568
TCT Ser	GCT Ala 185	Ası	n Ile	C ATO	ACA Thr	GAC Asp 186	Leu	GTC Val	TAC Tyr	CAG Gln	GGT Gly 186	Ala	AGC Ser	CTC	CAG Gln	5616
GCC Ala 1870	Gln	ACA	A GAO	C CGG P Arg	ACT Thr 187	Gly	GAG Glu	ATG Met	GCC Ala	CTG Leu 1880	His	CTT Leu	GCA Ala	GCC Ala	CGC Arg 1885	5664
TAC Tyr	TCA Ser	CGG	GCT Ala	GAT Asp 189	Ala	GCC	AAG Lys	CGT Arg	CTC Leu 1895	Leu	GAT Asp	GCA Ala	GGT Gly	GCA Ala 190	Asp	5712
GCC Ala	AAT Asn	GCC	Glr 190	GAC Asp 5	AAC Asn	ATG Met	GGC	CGC Arg 1910	Cys	CCA Pro	CTC Leu	CAT His	GCT Ala 191	Ala	GTG Val	5760
GCA Ala	GCT Ala	GAT Asp 192	Ala	CAA Gln	GGT Gly	GTC Val	TTC Phe 1925	Gln	ATT Ile	CTG Leu	ATT Ile	CGC Arg 1930	Asn	CGA Arg	GTA Val	5808
Thr .	GAT Asp 1935	Leu	GAT Asp	GCC	AGG Arg	ATG Met 1940	Asn	GAT Asp	GGT Gly	Thr	ACA Thr 1945	Pro	CTG Leu	ATC Ile	CTG Leu	5856
GCT Ala 1950	Ala	CGC Arg	CTG Leu	GCT Ala	GTG Val 1955	Glu	GGA Gly	ATG Met	Val .	GCA Ala 1960	Glu	CTG Leu	ATC Ile	AAC Asn	TGC Cys 1965	5904
CAA (Gln /	GCG Ala	GAT Asp	GTG Val	AAT Asn 1970	Ala	GTG Val	GAT (Asp :	CAT (His (GGA :	AAA Lys	TCT Ser	GCT Ala	CTT Leu 1980	His	5952

TGG GCA GCT Trp Ala Ala	GCT GTC Ala Val 1985	AAT AAT Asn Asn	GTG GAG Val Glu 1990	Ala Thr	CTT TTG Leu Leu	TTG TTG Leu Leu 1995	AAA 6000 Lys
AAT GGG GCC Asn Gly Ala 200	Asn Arg	Asp Met	CAG GAC Gln Asp 2005	AAC AAG Asn Lys	GAA GAG Glu Glu 2010	Thr Pro	CTG 6048 Leu
TTT CTT GCT Phe Leu Ala 2015	GCC CGG Ala Arg	GAG GGG Glu Gly 2020	Ser Tyr	GAA GCA Glu Ala	GCC AAG Ala Lys 2025	ATC CTG Ile Leu	TTA 6096 Leu
GAC CAT TTT Asp His Phe 2030	GCC AAT Ala Asn	CGA GAC Arg Asp 2035	ATC ACA Ile Thr	GAC CAT Asp His 2040	Met Asp	CGT CTT Arg Leu	CCC 6144 Pro 2045
CGG GAT GTG Arg Asp Val	GCT CGG Ala Arg 205	Asp Arg	ATG CAC Met His	CAT GAC His Asp 2055	ATT GTG Ile Val	CGC CTT Arg Leu 206	Leu
GAT GAA TAC Asp Glu Tyr	AAT GTG Asn Val 2065	ACC CCA	AGC CCT Ser Pro 2070	Pro Gly	ACC GTG. Thr Val	TTG ACT Leu Thr 2075	TCT 6240 Ser
GCT CTC TCA Ala Leu Ser 208	Pro Val	Ile Cys	GGG CCC Gly Pro 2085	AAC AGA Asn Arg	TCT TTC Ser Phe 2090	Leu Ser	CTG 6288 Leu
AAG CAC ACC Lys His Thr 2095	CCA ATG Pro Met	GGC AAG Gly Lys 2100	Lys Ser	AGA CGG Arg Arg	CCC AGT Pro Ser 2105	GCC AAG Ala Lys	AGT 6336 Ser
ACC ATG CCT Thr Met Pro 2110	ACT AGC Thr Ser	CTC CCT Leu Pro 2115	AAC CTT Asn Leu	GCC AAG Ala Lys 2120	Glu Ala	AAG GAT Lys Asp	GCC 6384 Ala 2125
AAG GGT AGT Lys Gly Ser	AGG AGG Arg Arg 2130	Lys Lys	TCT CTG Ser Leu	AGT GAG Ser Glu 2135	AAG GTC Lys Val	CAA CTG Gln Leu 2140	Ser
GAG AGT TCA Glu Ser Ser	GTA ACT Val Thr 2145	TTA TCC	CCT GTT Pro Val 2150	Asp Ser	CTA GAA Leu Glu	TCT CCT Ser Pro 2155	CAC 6480 His
ACG TAT GTT Thr Tyr Val 216	Ser Asp	Thr Thr	TCC TCT Ser Ser 2165	CCA ATG Pro Met	ATT ACA Ile Thr 2170	Ser Pro	GGG 6528 Gly
ATC TTA CAG Ile Leu Gln 2175	GCC TCA Ala Ser	CCC AAC (Pro Asn 1 2180	Pro Met	TTG GCC Leu Ala	ACT GCC Thr Ala 2185	GCC CCT Ala Pro	CCT 6576
GCC CCA GTC Ala Pro Val 2190	CAT GCC His Ala	CAG CAT (Gln His 2 2195	GCA CTA Ala Leu	TCT TTT Ser Phe 2200	Ser Asn	CTT CAT Leu His	GAA 6624 Glu 2205
ATG CAG CCT Met Gln Pro	TTG GCA Leu Ala 2210	His Gly	Ala Ser	ACT GTG Thr Val 2215	CTT CCC Leu Pro	TCA GTG Ser Val 2220	ser
CAG TTG CTA Gln Leu Leu	TCC CAC Ser His 2225	CAC CAC	ATT GTG Ile Val 2230	Ser Pro	GGC AGT Gly Ser	GGC AGT Gly Ser 2235	GCT 6720 Ala
GGA AGC TTG Gly Ser Leu 224	Ser Arg	Leu His	CCA GTC Pro Val 2245	CCA GTC Pro Val	CCA GCA Pro Ala 2250	Asp Trp	ATG 6768 Met

AAC CGC ATG GAG GTG AAT GAG ACC CAG TAC AAT GAG ATG TTT GGT ATG ABN Arg Met Glu Val Asn Glu Thr Gln Tyr Asn Glu Met Phe Gly Met 2255 2260 2265	6816
GTC CTG GCT CCA GCT GAG GGC ACC CAT CCT GGC ATA GCT CCC CAG AGC Val Leu Ala Pro Ala Glu Gly Thr His Pro Gly Ile Ala Pro Gln Ser 2270 2285	6864
AGG CCA CCT GAA GGG AAG CAC ATA ACC ACC CCT CGG GAG CCC TTG CCC Arg Pro Pro Glu Gly Lys His Ile Thr Thr Pro Arg Glu Pro Leu Pro 2290 2295 2300	6912
CCC ATT GTG ACT TTC CAG CTC ATC CCT AAA GGC AGT ATT GCC CAA CCA Pro Ile Val Thr Phe Gln Leu Ile Pro Lys Gly Ser Ile Ala Gln Pro 2305 2310 2315	6960
GCG GGG GCT CCC CAG CCT CAG TCC ACC TGC CCT CCA GCT GTT GCG GGC Ala Gly Ala Pro Gln Pro Gln Ser Thr Cys Pro Pro Ala Val Ala Gly 2320 2330	7008
CCC CTG CCC ACC ATG TAC CAG ATT CCA GAA ATG GCC CGT TTG CCC AGT Pro Leu Pro Thr Met Tyr Gln Ile Pro Glu Met Ala Arg Leu Pro Ser 2335 2340 2345	7056
GTG GCT TTC CCC ACT GCC ATG ATG CCC CAG CAG GAC GGG CAG GTA GCT Val Ala Phe Pro Thr Ala Met Met Pro Gln Gln Asp Gly Gln Val Ala 2350 2365	7104
CAG ACC ATT CTC CCA GCC TAT CAT CCT TTC CCA GCC TCT GTG GGC AAG Gln Thr Ile Leu Pro Ala Tyr His Pro Phe Pro Ala Ser Val Gly Lys 2370 2375 2380	7152
TAC CCC ACA CCC CCT TCA CAG CAC AGT TAT GCT TCC TCA AAT GCT GCT Tyr Pro Thr Pro Pro Ser Gln His Ser Tyr Ala Ser Ser Asn Ala Ala 2385	7200
GAG CGA ACA CCC AGT CAC AGT GGT CAC CTC CAG GGT GAG CAT CCC TAC Glu Arg Thr Pro Ser His Ser Gly His Leu Gln Gly Glu His Pro Tyr 2400 2405 2410	7248
CTG ACA CCA TCC CCA GAG TCT CCT GAC CAG TGG TCA AGT TCA TCA CCC Leu Thr Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Pro 2415 2420 2425	7296
CAC TCT GCT TCT GAC TGG TCA GAT GTG ACC ACC AGC CCT ACC CCT GGG His Ser Ala Ser Asp Trp Ser Asp Val Thr Thr Ser Pro Thr Pro Gly 2430 2445	7344
GGT GCT GGA GGA GGT CAG CGG GGA CCT GGG ACA CAC ATG TCT GAG CCA Gly Ala Gly Gly Gln Arg Gly Pro Gly Thr His Met Ser Glu Pro 2450 2455 2460	7392
CCA CAC AAC ATG CAG GTT TAT GCG TGAGAGAGTC CACCTCCAGT Pro His Asn Asn Met Gln Val Tyr Ala 2465 2470	7439
STAGAGACAT AACTGACTTT TGTAAATGCT GCTGAGGAAC AAATGAAGGT CATCCGGGAG	7499
AGAAATGAAG AAATCTCTGG AGCCAGCTTC TAGAGGTAGG AAAGAGAAGA TGTTCTTATT	7559
AGATAATGC AAGAGAAGCA ATTCGTCAGT TTCACTGGGT ATCTGCAAGG CTTATTGATT	7619
TTCTAATCT AATAAGACAA GTTTGTGGAA ATGCAAGATG AATACAAGCC TTGGGTCCAT	7679
TTTACTCTC TTCTATTTGG AGAATAAGAT GGATGCTTAT TGAAGCCCAG ACATTCTTGC	7739
GCTTGGACT GCATTTTAAG CCCTGCAGGC TTCTGCCATA TCCATGAGAA GATTCTACAC	7700

TAGCGTCCTG	TTGGGAATTA	TGCCCTGGAA	TTCTGCCTGA	ATTGACCTAC	GCATCTCCTC	7859
CTCCTTGGAC	ATTCTTTTGT	CTTCATTTGG	TGCTTTTGGT	TTTGCACCTC	TCCGTGATTG	7919
TAGCCCTACC	AGCATGTTAT	AGGGCAAGAC	CTTTGTGCTT	TTGATCATTC	TGGCCCATGA	7979
AAGCAACTTT	GGTCTCCTTT	CCCCTCCTGT	CTTCCCGGTA	TCCCTTGGAG	TCTCACAAGG	803
TTTACTTTGG	TATGGTTCTC	AGCACAAACC	TTTCAAGTAT	GTTGTTTCTT	TGGAAAATGG	8099
ACATACTGTA	TTGTGTTCTC	CTGCATATAT	CATTCCTGGA	GAGAGAAGGG	GAGAAGAATA	815
CTTTTCTTCA	ACAAATTTTG	GGGGCAGGAG	ATCCCTTCAA	GAGGCTGCAC	CTTAATTTTT	821
CTTGTCTGTG	TGCAGGTCTT	CATATAAACT	TTACCAGGAA	GAAGGGTGTG	AGTTTGTTGT	827
TTTTCTGTGT	ATGGGCCTGG	TCAGTGTAAA	GTTTTATCCT	TGATAGTCTA	GTTACTATGA	833
CCCTCCCCAC	TTTTTTAAAA	CCAGAAAAAG	GTTTGGAATG	TTGGAATGAC	CAAGAGACAA	839
GTTAACTCGT	GCAAGAGCCA	GTTACCCACC	CACAGGTCCC	CCTACTTCCT	GCCAAGCATT	845
CCATTGACTG	CCTGTATGGA	ACACATTTGT	CCCAGATCTG	AGCATTCTAG	GCCTGTTTCA	8519
CTCACTCACC	CAGCATATGA	AACTAGTCTT	AACTGTTGAG	CCTTTCCTTT	CATATCCACA	8579
GAAGACACTG	TCTCAAATGT	TGTACCCTTG	CCATTTAGGA	CTGAACTTTC	CTTAGCCCAA	8639
GGGACCCAGT	GACAGTTGTC	TTCCGTTTGT	CAGATGATCA	GTCTCTACTG	ATTATCTTGC	8699
TGCTTAAAGG	CCTGCTCACC	AATCTTTCTT	TCACACCGTG	TGGTCCGTGT	TACTGGTATA	875
CCCAGTATGT	TCTCACTGAA	GACATGGACT	TTATATGTTC	AAGTGCAGGA	ATTGGAAAGT	8819
TGGACTTGTT	TTCTATGATC	CAAAACAGCC	CTATAAGAAG	GTTGGAAAAG	GAGGAACTAT	8879
ATAGCAGCCT	TTGCTATTTT	CTGCTACCAT	TTCTTTTCCT	CTGAAGCGGC	CATGACATTC	893
CCTTTGGCAA	CTAACGTAGA	AACTCAACAG	AACATTTTCC	TTTCCTAGAG	TCACCTTTTA	8999
GATGATAATG	GACAACTATA	GACTTGCTCA	TTGTTCAGAC	TGATTGCCCC	TCACCTGAAT	9059
CCACTCTCTG	TATTCATGCT	CTTGGCAATT	TCTTTGACTT	TCTTTTAAGG	GCAGAAGCAT	911
TTTAGTTAAT	TGTAGATAAA	GAATAGTTTT	CTTCCTCTTC	TCCTTGGGCC	AGTTAATAAT	917
TGGTCCATGG	CTACACTGCA	ACTTCCGTCC	AGTGCTGTGA	TGCCCATGAC	ACCTGCAAAA	923
TAAGTTCTGC	CTGGGCATTT	TGTAGATATT	AACAGGTGAA	TTCCCGACTC	TTTTGGTTTG	929
AATGACAGTT	CTCATTCCTT	CTATGGCTGC	AAGTATGCAT	CAGTGCTTCC	CACTTACCTG	935
ATTTGTCTGT	CGCTGGCCCC	ATATGGAAAC	CCTGCGTGTC	TGTTGGCATA	ATAGTTTACA	941
AATGGTTTTT	TCAGTCCTAT	CCAAATTTAT	TGAACCAACA	AAAATAATTA	CTTCTGCCCT	9479
GAGATAAGCA	GATTAAGTTT	GTTCATTCTC	TGCTTTATTC	TCTCCATGTG	GCAACATTCT	953
GTCAGCCTCT	TTCATAGTGT	GCAAACATTT	TATCATTCTA	AATGGTGACT	CTCTGCCCTT .	9599
GGACCCATTT	ATTATTCACA	GATGGGGAGA	ACCTATCTGC	ATGGACCCTC	ACCATCCTCT	9659
GTGCAGCACA	CACAGTGCAG	GGAGCCAGTG	GCGATGGCGA	TGACTTTCTT	CCCCTGGGAA	971
TTCC	·		•			972

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising a therapeutically effective amount of a Notch protein; and a pharmaceutically acceptable carrier.

5

- 2. The composition of claim 1 in which the Notch protein is a human Notch protein.
- 3. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising an amino acid sequence encoded by the DNA sequence depicted in Figure 8A (SEQ ID NO:5), 8B (SEQ ID NO:6), 8C (SEQ ID NO:7), 9A (SEQ ID NO:8), or 9B (SEQ ID NO:9), which is able to be bound by an antibody to a Notch protein; and a pharmaceutically acceptable carrier.

15

20

- 4. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a Notch amino acid sequence depicted in Figure 8A (SEQ ID NO:5), 8B (SEQ ID NO:6), 8C (SEQ ID NO:7), 9A (SEQ ID NO:8), or 9B (SEQ ID NO:9), which displays one or more functional activities associated with a full-length Notch protein; and a pharmaceutically acceptable carrier.
- 5. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a fragment of a human Notch protein consisting essentially of the extracellular domain of the protein; and a pharmaceutically acceptable carrier.
- 6. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a region of a Notch protein containing the EGF homologous repeats of the protein; and a pharmaceutically acceptable carrier.

7. A pharmaceutical composition comprising a therapeutically effective amount of a fragment of a Notch protein lacking a portion of the EGF-homologous repeats of the protein, which fragment is able to be bound by an antibody to a Notch protein; and a pharmaceutically acceptable carrier.

5

15

- 8. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a functionally active portion of a Notch protein; and a pharmaceutically acceptable carrier.
- 9. The composition of claim 8 in which the Notch protein is a human Notch protein.
 - 10. A pharmaceutical composition comprising a therapeutically effective amount of a chimeric protein, said chimeric protein comprising a functionally active portion of a human Notch protein joined via a peptide bond to a sequence of a protein different from the Notch protein; and a pharmaceutically acceptable carrier.
- 11. The composition of claim 10 in which the functionally active portion of the Notch protein is encoded by the human cDNA sequence contained in plasmid hN3k as deposited with the ATCC and assigned accession number 68609, or encoded by the human cDNA sequence contained in plasmid hN5k as deposited with the ATCC and assigned accession number 68611.
- 25
 12. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising the amino acid sequence depicted in Figure 10 (SEQ ID NO:11); and a pharmaceutically acceptable carrier.
- 30 13. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising the amino acid sequence

ID: -WO

depicted in Figure 11 (SEQ ID NO:13); and a pharmaceutically acceptable carrier.

- 14. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising the portion of a human Notch protein with the greatest homology to the epidermal growth factor-like repeats 11 and 12 of the *Drosophila* Notch sequence as shown in Figure 4 (SEQ ID NO:14); and a pharmaceutically acceptable carrier.
- 15. A pharmaceutical composition comprising a therapeutically effective amount of a derivative or analog of a Notch protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Delta protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

15

16. A pharmaceutical composition comprising a therapeutically effective amount of a chimeric protein, said chimeric protein comprising a Notch protein joined via a peptide bond to a protein sequence of a protein different from the Notch protein; and a pharmaceutically acceptable carrier.

20

25

- 17. A pharmaceutical composition comprising a therapeutically effective amount of a fragment of a Notch protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Delta protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.
- 18. A pharmaceutical composition comprising a therapeutically effective amount of a chimeric protein, said chimeric protein comprising a fragment of a Notch protein joined via a peptide bond to a protein sequence of a protein different from the Notch protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Delta

protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

- 19. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a derivative or analog of a Delta protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.
- 20. A pharmaceutical composition comprising a therapeutically effective amount of a chimeric protein, said chimeric protein comprising a fragment of a Delta protein joined via a peptide bond to a protein sequence of a protein different from the Delta protein, which fragment is characterized by the ability in vitro, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.
- 21. A pharmaceutical composition comprising a therapeutically effective amount of a protein, said protein comprising a derivative or analog of a Serrate protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.
- 22. A pharmaceutical composition comprising a therapeutically effective amount of a derivative or analog of a Notch protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a second protein expressed on the surface of a second cell, which second protein is selected from the group consisting of a Delta protein and a Serrate protein; and a pharmaceutically acceptable carrier.

- 23. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a Notch protein; and a pharmaceutically acceptable carrier.
- 5 24. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a functionally active portion of a human Notch protein; and a pharmaceutically acceptable carrier.
- 25. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding the amino acid sequence depicted in Figure 10 (SEQ ID NO:11); and a pharmaceutically acceptable carrier.
- 26. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding the amino acid sequence depicted in Figure 11 (SEQ ID NO:13); and a pharmaceutically acceptable carrier.
 - 27. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a fragment of a Notch protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Delta protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.
- 28. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a chimeric protein, said chimeric protein comprising a functionally active fragment of a human Notch protein joined via a peptide bond to a protein sequence of a protein different from the Notch protein; and a pharmaceutically acceptable carrier.
- 29. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a fragment of a Delta protein, which fragment is characterized by the ability in vitro, when expressed on the surface of

a first cell, to bind to a Notch protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.

- : 30. A pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid encoding a fragment of a Serrate protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell; and a pharmaceutically acceptable carrier.
- 31. The composition of claim 24 in which the nucleic acid is a nucleic acid vector.
 - 32. A pharmaceutical composition comprising a therapeutically effective amount of an antibody which binds to a Notch protein; and a pharmaceutically acceptable carrier.
 - 33. A pharmaceutical composition comprising a therapeutically effective amount of a fragment or derivative of an antibody to a Notch protein containing the idiotype of the antibody; and a pharmaceutically acceptable carrier.

34. A method of treating or preventing a disease or disorder in a subject comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a molecule which antagonizes the function of a Notch protein.

25

20

15

35. The method according to claim 34 in which the disease or disorder is a malignancy characterized by increased Notch activity or increased expression of a Notch protein or of a Notch derivative capable of being bound by an anti-Notch antibody, relative to said Notch activity or expression in an analogous non-malignant sample.

- 36. The method according to claim 34 in which the disease or disorder is cervical cancer.
- 37. The method according to claim 34 in which the disease or5 disorder is breast cancer.
 - 38. The method according to claim 34 in which the disease or disorder is colon cancer.
- 39. The method according to claim 35 in which the malignancy is selected from the group consisting of melanoma, seminoma, and lung cancer.
 - 40. The method according to claim 35 in which the subject is a human.

15.

- 41. The method according to claim 36, 37 or 38 in which the molecule is an antibody to Notch or a portion of said antibody containing the binding domain thereof.
- 42. The method according to claim 36, 37 or 38 in which the molecule is a protein consisting of at least the extracellular domain of a Notch protein or a portion thereof capable of binding to a Notch ligand.
- 43. The method according to claim 36, 37 or 38 in which the molecule is a protein consisting of at least the EGF homologous repeats of a Notch protein.
- 44. The method according to claim 36, 37 or 38 in which the molecule is a protein consisting of at least an adhesive fragment of a Notch30 protein.

45. The method according to claim 36, 37 or 38 in which the molecule is an oligonucleotide which (a) consists of at least six nucleotides; (b) comprises a sequence complementary to at least a portion of an RNA transcript of a Notch gene; and (c) is hybridizable to the RNA transcript.

5

46. A method of treating or preventing a disease or disorder in a subject in need of such treatment or prevention comprising administering to the subject a therapeutically effective amount of a molecule which promotes the function of a Notch protein.

10

47. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a Notch protein.

15

- 48. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a functionally active portion of a Notch protein.
- 49. The method according to claim 47 in which the Notch protein 20 is a human Notch protein.
 - 50. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a chimeric protein, said protein comprising a functionally active portion of a Notch protein joined via a peptide bond to a protein sequence of a protein different from the Notch protein.
 - 51. The method according to claim 49 in which the human Notch protein comprises the amino acid sequence depicted in Figure 10 (SEQ ID NO:11) or Figure 11 (SEQ ID NO:13).

30

- 52. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a derivative or analog of a Notch protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a second protein expressed on the surface of a second cell, which second protein is selected from the group consisting of a Delta protein and a Serrate protein.
- 53. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a derivative or analog of a Delta protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell.
- 54. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a derivative or analog of a Serrate protein, which derivative or analog is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell.
 - 55. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a Notch protein.
- 56. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a functionally active portion of a Notch protein.
- 57. The method according to claim 55 in which the subject is human and the Notch protein is a human Notch protein.

- 58. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a fragment of a Notch protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a second protein expressed on the surface of a second cell, which second protein is selected from the group consisting of a Delta protein and a Serrate protein.
- 59. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a fragment of a Delta protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell.
- 60. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a nucleic acid encoding a fragment of a Serrate protein, which fragment is characterized by the ability *in vitro*, when expressed on the surface of a first cell, to bind to a Notch protein expressed on the surface of a second cell.
 - 61. A method of treating or preventing a malignancy in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of antibody to a Notch protein.
- 25 62. The method according to claim 58 in which the antibody is monoclonal.
- 63. A method for treating a patient with a tumor, of a tumor type characterized by expression of a <u>Notch</u> gene, comprising administering to the patient an effective amount of an oligonucleotide, which oligonucleotide (a) consists of at least six nucleotides; (b) comprises a sequence complementary to at

25

least a portion of an RNA transcript of the Notch gene; and (c) is hybridizable to the RNA transcript.

- 64. The method according to claim 60 in which the patient is ahuman, and the Notch gene is a human gene.
- 65. An isolated oligonucleotide consisting of at least six nucleotides, and comprising a sequence complementary to at least a portion of an RNA transcript of a Notch gene, which oligonucleotide is hybridizable to the
 10 RNA transcript.
 - 66. A pharmaceutical composition comprising the oligonucleotide of claim 65; and a pharmaceutically acceptable carrier.
 - 67. A method of inhibiting the expression of a nucleic acid sequence encoding a Notch protein in a cell comprising providing the cell with an effective amount of the oligonucleotide of claim 65.
- an aberrant level of Notch protein or activity in a patient, comprising measuring the level of Notch protein expression or activity in a sample derived from the patient, in which an increase or decrease in Notch protein or activity in the patient sample relative to the level found in such a sample from a normal individual indicates the presence of the disease or disorder in the patient.
 - 69. A method of diagnosing a malignancy characterized by an increased amount of a Notch protein or of a Notch derivative capable of being bound by an anti-Notch antibody, comprising measuring the amount of a Notch protein or of a Notch derivative capable of being bound by an anti-Notch antibody, in a sample containing or suspected of containing malignant cells from a patient, in which an increase in the amount of the Notch protein or of the Notch

derivative capable of being bound by an anti-Notch antibody, in the sample, relative to said amount found in an analogous sample of non-malignant cells indicates the presence of the disease or disorder in the patient.

- 5 70. The method according to claim 69 in which the malignancy is cervical cancer.
 - 71. The method according to claim 69 in which the malignancy is breast cancer.
 - 72. The method according to claim 69 in which the malignancy is colon cancer.
- 73. The method according to claim 69 in which the malignancy is selected from the group consisting of melanoma, seminoma, and lung cancer.
- 74. The method according to claim 69 in which the amount of the Notch protein or derivative is measured by a method comprising contacting the sample with an anti-Notch antibody such that immunospecific binding can occur,
 20 and measuring the amount of any immunospecific binding of the antibody that occurs.
 - 75. A method of treating or preventing a nervous system disorder in a subject comprising administering to a subject in need of such treatment or prevention an effective amount of a functionally active portion of a Notch protein.
 - 76. A method of promoting tissue regeneration or repair in a subject comprising administering to a subject an effective amount of a functionally active portion of a Notch protein.

- 77. A method of treating a benign dysproliferative disorder in a subject comprising administering to a subject in need of such treatment an effective amount of a functionally active portion of a Notch protein, in which the disorder is selected from the group consisting of cirrhosis of the liver, psoriasis, keloids, and baldness.
- 78. A substantially purified human Notch protein comprising the amino acid sequence encoded by the hN homolog as depicted in Figure 13 from amino acid numbers 1 through 2169 (SEQ ID NO:19).
- 79. A substantially purified human Notch protein comprising the amino acid sequence encoded by the hN homolog as depicted in Figure 13 from amino acid numbers about 26 through 2169 (as contained in SEQ ID NO:19).
- 15 80. A substantially purified protein comprising the extracellular domain of the mature human Notch protein encoded by the hN homolog, as depicted in Figure 13 from amino acid numbers about 26 through 1677 (as contained in SEQ ID NO:19).
- 20 81. A substantially purified protein comprising the EGF homologous repeats of the mature human Notch protein encoded by the hN homolog, as depicted in Figure 13 from amino acid numbers 26 through 1413 (as contained in SEQ ID NO:19).
- 25 82. A substantially purified protein comprising the EGF like repeats 11 and 12 of the mature human Notch protein encoded by the hN homolog, as depicted in Figure 13 (as contained in SEQ ID NO:19).
- 83. A substantially purified protein consisting essentially of the 30 extracellular domain of the mature human Notch protein encoded by the hN

15

homolog, as depicted in Figure 13 from amino acid numbers about 26 through 1677 (as contained in SEQ ID NO:19).

- 84. A substantially purified nucleic acid encoding the protein of5 claim 78.
 - 85. A substantially purified nucleic acid encoding the protein of claim 79.
- 10 86. A substantially purified nucleic acid encoding the protein of claim 80.
 - 87. A substantially purified nucleic acid encoding the protein of claim 82.

88. The nucleic acid of claim 85 which is a DNA molecule comprising the sequence depicted in Figure 17 from nucleotide numbers 82 through 7419 (as contained in SEQ ID NO:21).

- 89. The nucleic acid of claim 80 in which the sequence encoding the extracellular domain is as presented in Figure 17 (as contained in SEQ ID NO:21).
- 90. A recombinant cell containing the nucleic acid of claim 84, 87 or 88.
 - 91. The composition of claim 2 in which the Notch protein comprises the amino acid sequence encoded by the hN homolog as depicted in Figure 13 from amino acid numbers 26 through 2169 (as contained in SEQ ID NO:19).

30

5

- 92. A composition comprising a therapeutically effective amount of a Notch protein or Notch derivative, said derivative being capable of being bound by an anti-Notch antibody, for use as a medicament.
- 93. A composition comprising a therapeutically effective amount of a molecule which antagonizes the function of a Notch protein, for use as a medicament.
- 94. Use of a composition comprising a molecule which

 10 antagonizes the function of a Notch protein, for the manufacture of a medicament for the treatment of cervical cancer, breast cancer, or colon cancer.

15

20

25

30

GAATTCGGAG GAATTATTCA AAACATAAAC ACAATAAACA ATTTGAGTAG TTGCCGCACA	60
CACACACAC EACAGCCCGT GGATTATTAC ACTAAAAGCG ACACTCAATC CAAAAAATCA	120
GCAACAAAAA CATCAATAAA C ATG CAT TGG ATT AAA TGT TTA TTA ACA GCA Met His Trp Ile Lys Cys Leu Leu Thr Ala 1 5 10	171
TTC ATT TGC TTC ACA GTC ATC GTG CAG GTT CAC AGT TCC GGC AGC TTT Phe Ile Cys Phe Thr Val Ile Val Gln Val His Ser Ser Gly Ser Phe 15 20 25	219
GAG TTG CGC CTG AAG TAC TTC AGC AAC GAT CAC GGG CGG GAC AAC GAG Glu Leu Arg Leu Lys Tyr Phe Ser Asn Asp His Gly Arg Asp Asn Glu 30 35 40	267
GGT CGC TGC TGC AGC GGG GAG TCG GAC GGA GCG ACG GGC AAG TGC CTG Gly Arg Cys Cys Ser Gly Glu Ser Asp Gly Ala Thr Gly Lys Cys Leu 45 50 55	315
GGC AGC TGC AAG ACG CGG TTT CGC GTC TGC CTA AAG CAC TAC CAG GCC Gly Ser Cys Lys Thr Arg Phe Arg Val Cys Leu Lys His Tyr Gln Ala 60 65 70	363
ACC ATC GAC ACC ACC TCC CAG TGC ACC TAC GGG GAC GTG ATC ACG CCC Thr Ite Asp Thr Thr Ser Gln Cys Thr Tyr Gly Asp Val Ite Thr Pro 75 80 85 90	411
ATT CTC GGC GAG AAC TCG GTC AAT CTG ACC GAC GCC CAG CGC TTC CAG le Leu Gly Glu Asn Ser Val Asn Leu Thr Asp Ala Gln Arg Phe Gln 95 100 105	459
AAC AAG GGC TTC ACG AAT CCC ATC CAG TTC CCC TTC TCG TTC TCA TGG ASN Lys Gly Phe Thr Asn Pro Ile Gln Phe Pro Phe Ser Phe Ser Trp 110 115 120	507

FIG.1A

			Phe		CTG Leu			Glu								555
AGC Ser	GGC Gly 140	AAT Asn	GCG Ala	CGA Arg	ACC Thr	AAC Asn 145	AAG Lys	CTC Leu	CTC Leu	ATC Ile	CAG Gln 150	CGA Arg	CTC Leu	TTG Leu	GTG Val	603
					GTG Val 160											651
					CTG Leu											699
					GGC Gly											747
TCA Ser	TTT Phe	GGA Gly 205	CAC His	TCG Ser	ACT Thr	TGC Cys	TCG Ser 210	GAG Glu	ACG Thr	GGC Gly	GAA Glu	ATT I le 215	ATC I le	TGT Cys	TTG Leu	795
ACC Thr	GGA Gly 220	TGG Trp	CAĢ Gln	GGC Gly	GAT Asp	TAC Tyr 225	TGT Cys	CAC His	ATA Ile	CCC Pro	AAA Lys 230	TGC Cys	GCC Ala	AAA Lys	GGC Gly	843
					TGC Cys 240											891
GGC Gly	TGG Trp	AAG Lyş	Gly	GCC Ala 255	TTG Leu	TGC Cys	AAC Asn	Glu	TGC Cys 260	GTT Val	CTG Leu	GAA Glu	CCG Pro	AAC Asn 265	TGC Cys	939

FIG.1B

SUBSTITUTE SHEET (RULE 26)

3/68 ATC CAT GGC ACC TGC AAC AAA CCC TGG ACT TGC ATC TGC AAC GAG GGT Ile His Gly Thr Cys Asn Lys Pro Trp Thr Cys Ile Cys Asn Glu Gly TGG GGA GGC TTG TAC TGC AAC CAG GAT CTG AAC TAC TGC ACC AAC CAC Irp Gly Gly Leu Tyr Cys Asn Gln Asp Leu Asn Tyr Cys Thr Asn His AGA CCC TGC AAG AAT GGC GGA ACC TGC TTC AAC ACC GGC GAG GGA TTG Arg Pro Cys Lys Asn Gly Gly Thr Cys Phe Asn Thr Gly Glu Gly Leu TAC ACA TGC AAA TGC GCT CCA GGA TAC AGT GGT GAT GAT TGC GAA AAT Tyr Thr Cys Lys Cys Ala Pro Gly Tyr Ser Gly Asp Asp Cys Glu Asn GAG ATC TAC TCC TGC GAT GCC GAT GTC AAT CCC TGC CAG AAT GGT GGT Glu Ile Tyr Ser Cys Asp Ala Asp Val Asn Pro Cys Gln Asn Gly Gly ACC TGC ATC GAT GAG CCG CAC ACA AAA ACC GGC TAC AAG TGT CAT TGC Thr Cys Ile Asp Glu Pro His Thr Lys Thr Gly Tyr Lys Cys His Cys GCC AAC GGC TGG AGC GGA AAG ATG TGC GAG GAG AAA GTG CTC ACG TGT Ala Asn Gly Trp Ser Gly Lys Met Cys Glu Glu Lys Val Leu Thr Cys TCG GAC AAA CCC TGT CAT CAG GGA ATC TGC CGC AAC GTT CGT CCT GGC Ser Asp Lys Pro Cys His Gln Gly Ile Cys Arg Asn Val Arg Pro Gly TTG GGA AGC AAG GGT CAG GGC TAC CAG TGC GAA TGT CCC ATT GGC TAC Leu Gly Ser Lys Gly Gln Gly Tyr Gln Cys Glu Cys Pro Ile Gly Tyr

FIG.1C

AGC Ser	GGA Gly	CCC Pro	AAC Asn	TGC Cys 415	GAT Asp	CTC Leu	CAG Gln	CTG Leu	GAC Asp 420	AAC Asn	TGC Cys	AGT Ser	CCG Pro	AAT Asn 425	CCA Pro	1419
TGC Cys	ATA I le	AAC Asn	GGT Gly 430	GGA Gly	AGC Ser	TGT Cys	CAG Gln	CCG Pro 435	AGC Ser	GGA Gly	AAG Lys	TGT Cys	ATT Ile 440	TGC Cys	CCA Pro	1467
GCG	GGA Gly	TTT Phe 445	TCG Ser	GGA Gly	ACG Thr	AGA Arg	TGC Cys 450	GAG Glu	ACC Thr	AAC Asn	ATT	GAC Asp 455	GAT Asp	TGT Cys	CTT Leu	1515
Gly	CAC His 460	CAG Gln	TGC Cys	GAG Glu	AAC Asn	GGA Gly 465	GGC Gly	ACC Thr	TGC Cys	ATA Ile	GAT Asp 470	ATG Met	GTC Val	AAC Asn	CAA Gln	1563
TAT Tyr 475	CGC Arg	TGC Cys	CAA Gln	TGC Cys	GTT Val	CCC Pro 480	GGT Gly	TTC Phe	CAT His	GGC G l y 485	ACC Thr	CAC His	TGT Cys	AGT Ser	AGC Ser 490	1611
AAA Lys	GTT Val	GAC Asp	TTG Leu	TGC Cys 495	CTC Leu	ATC I le	AGA Arg	CCG Pro	TGT Cys 500	GCC Ala	AAT Asn	GGA Gly	GGA Gly	ACC Thr 505	TGC Cys	1659
TTG Leu	AAT Asn	CTC Leu	AAC Asn 510	AAC Asn	GAT Asp	TAC Tyr	CAG Gln	TGC Cys 515	ACC Thr	TGT Cys	<u>C</u> GT Arg	GCG Ala	GGA Gly 520	TTT Phe	ACT Thr	1707
GGC Gly	AAG Lys	GAT Asp 525	TGC Cys	TCT Ser	GTG Val	GAC Asp	ATC I le 530	GAT Asp	GAG Glu	TGC Cys	AGC Ser	AGT Ser 535	GGA Gly	CCC Pro	TGT Cys	1755
CAT His	AAC Asn 540	GGC Gly	GGC Gly	ACT Thr	TGC Cys	ATG Met 545	AAC Asn	CGC Arg	GTC Val	AAT Asn	TCG Ser 550	TTC Phe	GAA Glu	TGC Cys	GTG Val	1803

FIG.1D

SUBSTITUTE SHEET (RULE 26)

				CGAT GAG GAG Asp Glu Glu 565		
		Ala His Gl		GCG ACC ACA Ala Thr Thr		
				CTA ATT GCT Leu Ile Ala		
Val Ala Mo			l Ile Ala	GCG TGC GTG Ala Cys Val 615		
				AAG GAC GAC Lys Asp Asp 630		
	n Asn Glu		Val Ala	ACA ATG CAT Thr Met His 645	His Asn (
				TCT CTG GGC (Ser Leu Gly (
GGC AGC AAI Gly Ser Asi	C AGC GGT (n Ser Gly 1 670	CTC ACC TTC _eu Thr Phe	GAT GGC Asp Gly (675	GGC AAC CCG A Gly Asn Pro A	AAT ATC A Asn Ile I 880	TC 2187 le
	· Trp Asp L			ATT TGT GCC T The Cys Ala S 695		

FIG.1E

6/68 GCA GCG GCG GCG GCA GCA GCG GCG GAC GAG TGT CTC ATG TAC GGC Ala Ala Ala Ala Ala Ala Ala Ala Asp Glu Cys Leu Met Tyr Gly GGA TAT GTG GCC TCG GTG GCG GAT AAC AAC AAT GCC AAC TCA GAC TTT Gly Tyr Val Ala Ser Val Ala Asp Asn Asn Asn Ala Asn Ser Asp Phe TGT GTG GCT CCG CTA CAA AGA GCC AAG TCG CAA AAG CAA CTC AAC ACC Cys Val Ala Pro Leu Gln Arg Ala Lys Ser Gln Lys Gln Leu Asn Thr GAT CCC ACG CTC ATG CAC CGC GGT TCG CCG GCA GGC AGC TCA GCC AAG Asp Pro Thr Leu Met His Arg Gly Ser Pro Ala Gly Ser Ser Ala Lys GGA GCG TCT GGC GGA GGA CCG GGA GCG GCG GAG GGC AAG AGG ATC TCT Gly Ala Ser Gly Gly Gly Pro Gly Ala Ala Glu Gly Lys Arg Ile Ser GIT TTA GGC GAG GGT TCC TAC TGT AGC CAG CGT TGG CCC TCG TTG GCG Val Leu Gly Glu Gly Ser Tyr Cys Ser Gln Arg Trp Pro Ser Leu Ala GCG GCG GGA GTG GCC GGA GCC TGT TCA TCC CAG CTA ATG GCT GCA GCT Ala Ala Gly Val Ala Gly Ala Cys Ser Ser Gln Leu Met Ala Ala Ala Ser Ala Ala Gly Ser Gly Ala Gly Thr Ala Gln Gln Gln Arg Ser Val GTC TGC GGC ACT CCG CAT ATG TAACTCCAAA AATCCGGAAG GGCTCCTGGT Val Cys Gly Thr Pro His Met AAATCCGGAG AAATCCGCAT GGAGGAGCTG ACAGCACATA CACAAAGAAA AGACTGGGTT GGGTTCAAAA TGTGAGAGAG ACGCCAAAAT GTTGTTGTTG ATTGAAGCAG TTTAGTCGTC ACGAAAAATG AAAAATCTGT AACAGGCATA ACTCGTAAAC TCCCTAAAAA ATTTGTATAG TAATTAGCAA AGCTGTGACC CAGCCGTTTC GATCCCGAAT TC

FIG.1F SUBSTITUTE SHEET (RULE 26)

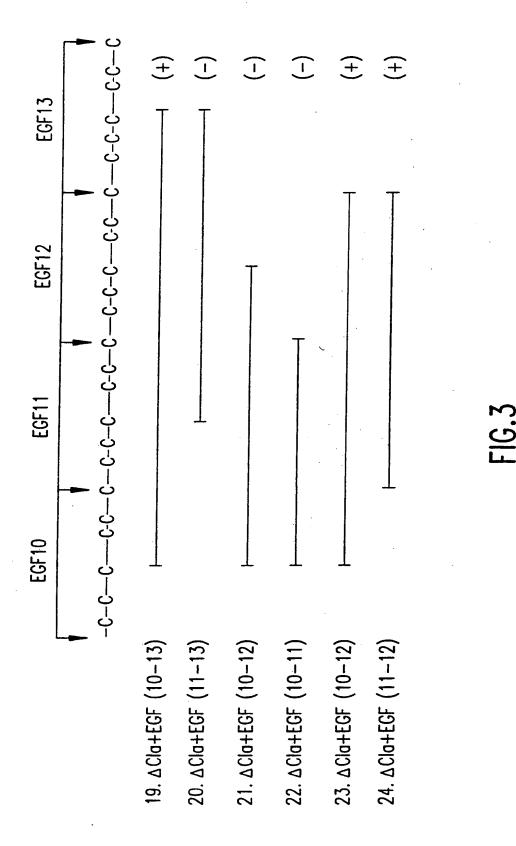
WO 94/07474 PCT/US93/09338

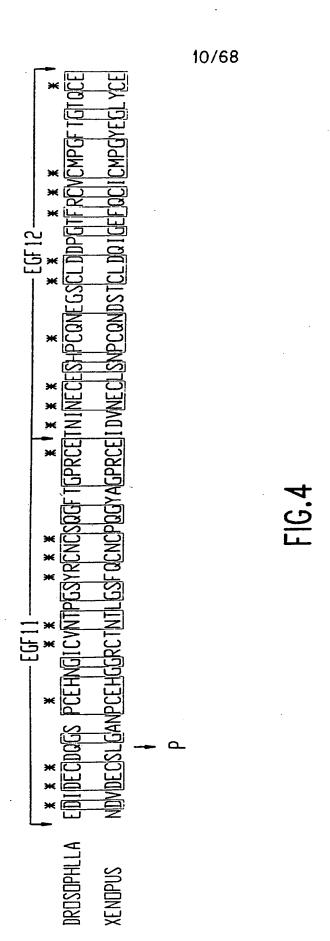
	7/68 % AGGREGATION	
1.pMtNMg	TM WITH DI WITH Ser SP EGF N cdc10 PA opa THEOREM THE PARTY SERVICE	
. 2.△Sph	1 32 0 nt	
3.△Cla	7 31 0 nt	
4.△EGF(7-17)	7 17	
5.△EGF(9-26)	9 26 mm	
6.△EGF(17-30)	17 31 22 nt	
7.△EGF(7-9)	7 9 	
8.△EGF(9-17)	9 17 FIG.2	2A
9.△EGF(17-26)	17 26 10 8	
10.△EGF(26-30)	26 31 	
11.△EGF(9-30)	9 31 0 nt	
12.△EGF(7-26)	7 26 0 nt	
13.△ Cla+EGF(9-17)	7 9 17 31 	٠
14.△Clo+EGF(17-26)	7 17 26 31 0 nt	
15.SPLIT	14 12 nt	
16.△ Clo+EGF(9-13)	7 9 13 31 47 25	

SUBSTITUTE SHEET (RULE 26)

8/68 7 11 15 31 0 0 17.△Clo+EGF(11-15) □□□□ □□□ 7 13 17 31 0 nt 71013 31 19. △Clo+EGF(10-13) [] [] [] H 56 23 71113 31 0 nt 7 1012 31 0 21. △Clo+EGF(10-12) □□□□□ □□ nt 7 1011 31 0 nt 7 1012 31 45 nt 7 1112 31 24. △Clo+EGF(11-12) □□□□□ □□□□ 11 nt 25. △EGF 0 nt FIG.2B \mathbb{H} Ш 9 17 26. △EGF+EGF(9-17) 24 nt 9 13 40 27. △EGF+EGF(9-13) nt \mathbf{m} 1013 23 28. △EGF+EGF(10-13) III 45 1012 29. △EGF+EGF(10-12) Ⅲ 48 nt 1 0 nt 30. △ECN 1013 26 31. △ ECN+EGF(10-13) □□ nt 1012 47 22 32. △ECN+EGF(10-12) □□ 00 20 42 33. △Clo+XEGF(10-13) □□□□□

SUBSTITUTE SHEET (RULE 26)





CGCGATTGTCGATCATTAAAGTCTGCCTGCAACTTAATTGCTTTAATTTTAATACTGTTA ArgAspCysArgSerLeuLysSerAlaCysAsnLeuTTeATaLeuTTeLeuTTeLeuT

AACAGCCATCTACTCAACGGCTATTGCTGCGGCATGCCAGCGGAACTTAGGGCCACCAAG AsnSerHisLeuLeuAsnGlyTyrCysCysGlyMetProAlaGluLeuArgAlaThrLys

1CGTCGTTGGAGTCAACAATAGAATCAGCAGACAGCCTGGGAATGTCCAAGAAGACGGCG

481

601

SerSerLeuGluSerThrIleGluSerAlaAspSerLeuGlyMetSerLysLysThrAla

ACCIGAGCAGGGTGCCAGCATATCCACGGGCTGTTCGTTTGGCAACIGCCACCACCAGATA Thr|GluGlnGlyAlaSerIleSerThrGlyCysSerPheGlyAsn|AlaThr_ThrLysIle

ACGITICGITGGACGAAGICGITIACGCIGATACIGCAGGCGITGGAIAIGIACAACACA ThrPheArgTrpThrLysSerPheThrLeuIleLeuGInAlaLeuAspMetTyrAsnThr 961

TCGCCGGAGTGGAAGACGCTGGACCACATCGGGCGGAACGCGCGGATCACCTACCGTGTC SerProGluTrpLysThr|LeuAspHisIleGlyArgAsnAlaArgIleThrTyrArgVal GACGATCAGTTCGGTCAQTACGCCTGCGGCTCCGAGGGTCAGAAGCTCTGCCTGAATGGC AspAspGInPheGIyH; \$TyrAlaCysGIySerGIuGIyGInLysLeuCysLeuAsnGIy 1201

SUBSTITUTE SHEET (RULE 26)

721

841

241

CCGAGTCGAGCGCCGTGCTTCGAGCGGTGATGAGCCCCTTTTCTGTCAACGCTAAAGATC CAATCCAGAGTGAATCCGAAACAAACTCCATCTAGATCGCCAACCAGCATCACGCTCGCA

3 MetPheArgLysHisPheArgArgLysProAlaThrSer AACGCCCCCAGAATGTACAAATGTTTAGGAAACATTTTCGGCGAAAACCAGCTACGTCG CCAAACAAAACCAAAACGAAGGCAAAGTGGAGAAATGATACAGCATCCAGAGTAC CCAAAATCTGCATACATGGGCTAATTAAGGCTGCCCAGCGAATTTACATTTGTGTGGTGC

23 ThrLysArgGinArgProArgHisArgVaiProLysIleAlaThrLeuProSerThrIle ACAAAAAGGCAGCGTCCGAGGCATCGGGTACCCAAAATCGCGACCCTGCCATCGACGATC

93 ValHisLysIleSerAlaAlaGlyAsnPheGluLeuGluIleLeuGluIleSerAsnThr <u>GTCCATAAGATATCCGCAGCTGGTAACTTCGAGCTGGAAATATTAGAAATCTCAAATACC</u>

133 Thr!leGlyCysSerProCysThrThrAldPheArgLeuCysLeuLysGluTyrGlnThr ACGATAGGCTGCTCGCCATGCACGACGGC4TTCCGGCTGTGCCTGAAGGAGTACCAGACC

173 LeuGlyGlySerSerPheValLeuSerAspProGlyValGlyAlaIleValLeuProPhe CTGGGTGGCTCCAGQTTTGTGCTCAGCGATCCGGGTGTGGGAGCCATTGTGCTGCCCTTT

SerTyrProAspAlaGluArgLeuIleGluGluThrSerTyrSerGlyValIleLeuPro fccTaTcCaGaTGCGGAGGTTAATTGAGGAAACATCATACTGGGGCGTGATACTGCCG

253 ArgValGinCysAlaValThrTyrTyrAsnThrThrCysThrThrPhqCysArgProArg CGGGTGCAATGCGCCGTTACCTACTACAACACGACCTGCACGACCTTQTGCCGTCCGCGG

293 TGGCAGGGCGTCAACTGCGAGGAGGCCATATGCAAGGCGGGCTGCGACCCCGTCCACGGC TrpGinGiyVaiAsnCysGiuGiuAialieCysLysAiaGiyCysAspProVaiHisGiy

FIG 5F

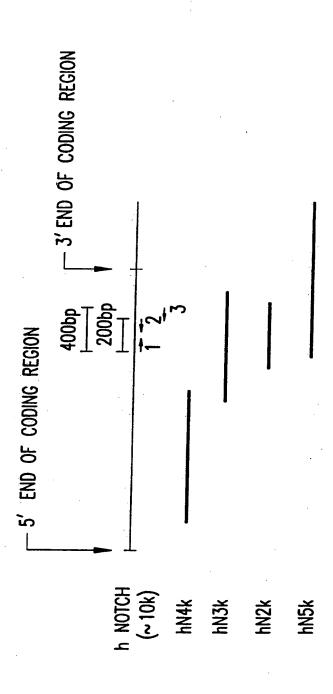
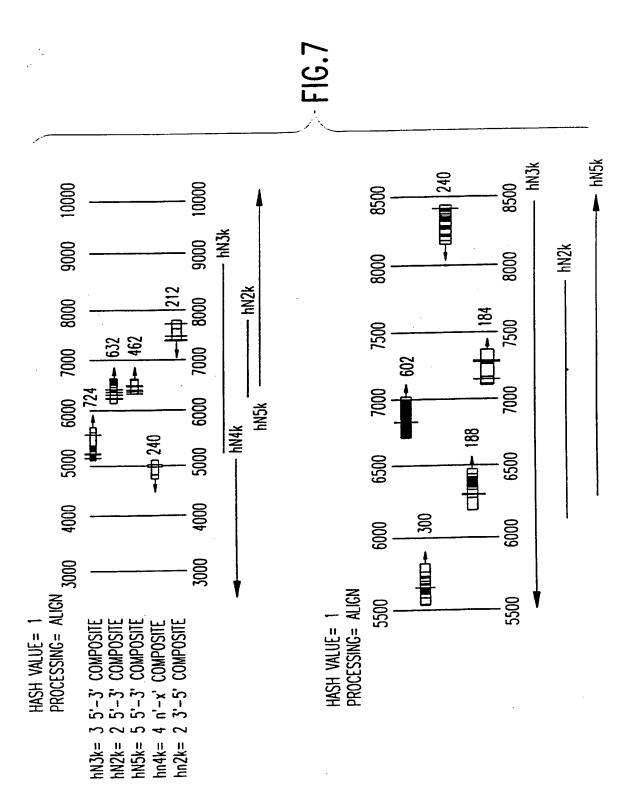


FIG. 6



GAATTCCGCT GGGAGAATGG TCTGAGCTAC CTGCCCGTCC TGCTGGGGCA TCAATGGCAA
GTGGGGAAAG CCACACTGGG CAAACGGGCC AGGCCATTTC TGGAATGTGG TACATGGTGG
121 GCAGGGGGCC CGCAACAGCT GGAGGGCAGG TGGACTGAGG CTGGGGATCC CCCGCTGGTT
181 GGGCAATACT GCCTTTACCC ATGAGCTGGA AAGTCACAAT GGGGGGCAAG GGCTCCCGAG
241 GGTGGTTATG TGCTTCCTTC AGGTGGC

FIG.8A

1 GAATTCCTTC CATTATACGT GACTTTTCTG AAACTGTAGC CACCCTAGTG TCTCTAACTC 61 CCTCTGGAGT TTGTCAGCTT TGGTCTTTTC AAAGAGCAGG CTCTCTTCAA GCTCCTTAAT GCGGGCATGC TCCAGTTIGG TCTGCGTCTC AAGATCACCT TTGGTAATTG ATTCTTCTTC 121 AACCCGGAAC TGAAGGCTGG CTCTCACCCT CTAGGCAGAG CAGGAATTCC GAGGTGGATG 181 TGTTAGATGT GAATGTCCGT GGCCCAGATG GCTGCACCCC ATTGATGTTG GCTTCTCCC 241 GAGGAGGCAG CTCAGATTTG AGTGATGAAG ATGAAGATGC AGAGGACTGT TCTGCTAACA 301 TCATCACAGA CTTGGTCTAC CAGGGTGCCA GCCTCCAGAC CAGACAGACC GGACTGGTGA 361 421 GATGGCCCTG CACCTTGCAG CCCGCTACTC ACGGGCTGAT GCTGCCAAGC GTCTCCTGGA TGCAGGTGCA GATGCCAATG CCCAGGACAA CATGGGCCGC TGTCCACTCC ATGCTGCAGT GGCACGTGAT GCCAAGGTGT ATTCAGATCT GTTA 541

FIG.8B

1 TCCAGATTCT GATTCGCAAC CGAGTAACTG ATCTAGATGC CAGGATGAAT GATGGTACTA
61 CACCCCTGAT CCTGGCTGCC CGCCTGGCTG TGGAGGGAAT GGTGGCAGAA CTGATCAACT
121 GCCAAGCGGA TGTGAATGCA GTGGATGACC ATGGAAAATC TGCTCTTCAC TGGGCAGCTG
181 CTGTCAATAA TGTGGAGGCA ACTCTTTTGT TGTTGAAAAA TGGGGCCAAC CGAGACATGC
241 AGGACAACAA GGAAGAGACA CCTCTGTTTC TTGCTGCCCG GGAGGAGCTA TAAGC

FIG.8C

GAATTCCATT CAGGAGGAAA GGGTGGGGAG AGAAGCAGGC ACCCACTTTC CCGTGGCTGG
ACTCGTTCCC AGGTGGCTCC ACCGGCAGCT GTGACCGCCG CAGGTGGGGG CGGAGTGCCA
TTCAGAAAAT TCCAGAAAAG CCCTACCCCA ACTCGGACGG CAACGTCACA CCCGTGGGTA
GCAACTGGCA CACAAACAGC CAGCGTGTCT GGGGCACGGG GGGATGGCAC CCCCTGCAGG
CAGAGCTG

FIG.9A

1 CTAAAGGAA CAAAAGCNGG AGCTCCACCG CGGGCGGCNC NGCTCTAGAA CTAGTGGANN
61 NCCCGGGCTG CAGGAATTCC GGCGGACTGG GCTCGGGCTC AGAGCGGCGC TGTGGAAGAG
121 ATTCTAGACC GGGAGAACAA GCGAATGGCT GACAGCTGGC CTCCAAAGTC ACCAGGCTCA
181 AATCGCTCGC CCTGGACATC GAGGGATGCA GAGGATCAGA ACCGGTACCT GGATGGCATG
241 ACTCGGATTT ACAAGCATGA CCAGCCTGCT TACAGGGAGC GTGANNTTTT CACATGCAGT
301 CGACAGACAC GAGCTCTATG CAT

FIG.9B

FIG. 10A

			1												
240	*	GAC	^			TGC	ô		*	GTA	\$			CCG	
	*	TAC	>-		*	ည္ဟ	_U			G CAT G	Ħ	380	-k	3 ATG	Σ
		CIG		0	*	CAG	a	330	*	GAG	ធ			CH	Ы
230	*	CCC	Δι	280		GAC	Ω		*	929	æ			GIG	
2		: AAC	Z		*	IGC	ပ			C TGT G	O	70	*	GTG	>
	*	IGC	O .			CAC	I	320	*	A,		370		GTG	>
	*	CAG		270	*	999	ტ	(*)		CTG	h			GIG	
220		၁၅၅			*	GAC	Ω		*	999	U			CTG	L
	*	GAA				AGC	တ	0	*	SAC	Ω	360	*	ACG	
		909	K	09	*	CAC ITC	[Li	33		TGG	<u>γ</u>		*	ည	G
210	*	GT GCG	%	(7)		CAC	工		*	GAG	ា			ည္ဟ	K
	*	CAG	ø		*	GAC	Ω			TGC	ပ	350	*	ဗ္ဗဘ္ဗ	Æ
		TGC	ပ	0.0	*	AAG	×	300	*	GAG	យ				니
200	k	GAC	Ω	250			U		*		K		*		ĸ
2		TIT	Ŀı		*∙	TAC	>-			AGC	တ	340	*		ы
	*	CGC	U			CAG	ø	290	*	AAC	z	ψ.		SSS	Ωı

F16,108

30	AGC S>	480 4 * Q	55 5	+ E 7
4	CTC AG	့ * ဗ	AAG K	CIG
	GAG E	CAC	20 CGC	570 * GCC
	CGG R	470 * C GCA	520 * CTG CG	GAC D
420	CIG	G.A.	# CAG	CCT
4	TTC	CGT R	GAG	560 * GCA
	CAC	460 * * GTC TTC AAG C	510 * GAG E	000 A
410	TTC	TIC	* 00 %	7 7 3 X
	TCC	* GTC	ည ည	0; 0; 0;
*	AGC S	GTG	500 * TAC	550 646 GG
00	AAC	450 * AAC N	TAC	* GC *
4	G CGC AAC	* ACC	* 000	900 A
#	HH	S H	490 FC TTC	540 * CGT R
	CAG O	440 ** CTG	ATC I	* 5 X AAG C K
390	GAG	GTG V	ATG M	ATC
*	P P	* 50 %	CAG	530 CCC

FIG. 10C

620 GGG CGG G RS 670 V YS V YS TGC TTC C FS GAG GGT (
E G G
TCC ATC |
TCC ATC |
TCG CAG
TCG CAG
S TCG CAG
S TCG CAG
TCG CA 600 CTC CCT GGT G L P G 650 ATG GAC GTC C M D V 700 * 700 C V Q C C V Q C C V Q C C N Q C T T C CTG C 580 GGC CAG G Q 630 * CGG CGG

FIG. 10D

F16.10E

	GAG E>	* 55 V	AAG X	CAG CAG
•	* ၁၅၅	SCC A	.00 * ACC	1150 * GAC CA D Q
00	CIC	1050 * GGT	1100 AGAGACC E T	GAC D
1000	CCC P	GAC D	CTG *	CIG
+	GAG	TCA	90 * GAC	1140 * GAC
	CGG R	1040 * AAC GCT	1090 * GAG GA E D	ccr P
986	, 000 R	1(AAC N	GAC D	CIG
*	AAG	AAG K	9 9 0	130 * GTT V
	AAG	30 * CTG L	1080 * ; TGG	11. Grg (
980	AAG K	1030 * CCC CT	CAG B B	* D &
	AGC S	AAG K	AAT	20 * GAG
*	SCC A	CIC	0 * 4 Q	11 GAG
970	GAG E	1020 * 3 GGC (AAC N	* TT =
	TCT	* GTC >	GAC D	CGG R
*	GTG V	TCC S	60 * GAC D	11110 TTC F
	AAA (010 * GAC D	1060 * ATG G2	* AAG

FIG. 10 F

55.7 * CTC 1340 1290 TTC ACC CCG F T P 1190 CAG GGT 0 0 0 1280 * CCT GAT P D 1230 * CCC (CAG CAC * **5**55 , \$22 800 8 1270 AAT GTC CGC N V R 1320 * * GGG GGC 1220 GCC CCC A P 1210 * * TCT GCC ATG G 1260 * ATG GAC GTC A M D V * CGC ATG R M

F16.106

0	*	255	Ġ	1440	+	CAC	仝			GAG	습		*	CTG	3
139) 	CAG GG	Ø	7	*	TTG	H		*	CTG	H			SSS	م
		TAC	¥			SCC	A	30	*	CTG	u	1530) *))	ACC	
		ATC	Н	130	*	ACC	Ę	148		ည္ပ	R		*	ည္ပ	rc.
.380	*	TTC	[L	1430		GAG	េ			AAG		•		S	
-	*	GAC			*	$\mathcal{G}_{\mathcal{G}}$	U			၁၁၅		520	*	AAC ATG	Σ
		TCC	ഗ	20	*	ACG	₽	1470	*	GAT GCC	K	<u>-</u> -		AAC	z
370	*	GTC ATC	ц	1420		ည္သည	ĸ	•	*	GAT	Ω		*	GAC	Ω
		GTC	>			GAC				TCT	ഗ	2	*	CAG	a
		ည				ACA	Ę⊸i	160	*	\mathcal{G}	S R	1510		ATC	Н
20	*	555	Zi.	1410	#	CAG	a	Ä		TCA	လ		*	AAC	z
136		22 525	⋖	•	*	AAC	Z		*	TAC	×			ည	A
	*	GAC				5	II.	20	*	ညည	æ	1500	*	GAT	Ω
		GAG G	ม	1400	k	CTG	J	1450		000	K		*	5	K
1350	*	GAG	ม	1,		AGC			*	ညည	K			AGC	
-7	*	GAA	ม	-	k	ပ္ပင္ပ	4			CIG	ᆸ	1490	*	၁၁၅	K

FIG. 10H

FIG. 10 I

1870 * * * TAC GAG ACC GCC Y E T A> 1920 * * CAT ATG H M> GAC D 1910 * * * * G GAC ATC ACG GAT C D I T D 1860 * * GGC AGC 1 G S 1800 * F AAC AAA N K * 225 A t 1940 CGC GAC ATC R D I 1840 CTG TTT CTG (L F L 1890 * 1890 CTG GAC CAC T CTG AAG AAC GGG L K N G 1790 1880 * AAG GTG CTG (K V L 1830 * * * GAG ACA CCC C E T P 1780 GTG CTC V L

FIG. 10J

FIG. 10X

	ξ ι γ	* 57 8	TCC	× × ATG
	* UU U	GAG		2350 * GGG AT G E
0	AAG K	2250 * : CTG	2300 CTG CCC	* CC 4
2200	ည္ပမ	္ ဦး ေ	CHG *	CIG
	GAT D	GAC	90 * CCA	2340 * : CAC
	CAG O	.40 * GTG	2290 * CCG CC	AAC N
190	TCC S	22, CCC (* TC &	CTC
,	AAG	. S	A GC	2330 GTG CCC
	AAG		2280 • GTG	2.616
180	CGG AGG	2230 ATG CT M I	GAC D	* TCC
	_	* ပ္ပံ ဗ	TCA S	20 * CCG
4	, Ω ≪	JCC S	270 * CTG	2320 * TCT CC
0 +	CIC AAG L K	2220 * : AGC	22 TAC Y	* CAG
2170	CIC	GAC	* ပ္ပံ ဗ	CAG
*	G GAC (CIG	60 * CAT	2310 G TTC
,	AAG	2210 * CTG L	2260 * CCC C	* 55 4

FIG. 10L

2400	* CCC *	9 6	* GTC	TC SV
•	AAG K	ACT *	ACC	.40 .40 .666
	DCC	10 GAG E	2490 * : AGC S	2540 * 66C 666 6 6
2390	* GCG	2440 * TIT G	* ACC	* GIG >
2	GTG	* 900 ×	ပ္ပ ဗ	30 * ACT
	AAC N	CIG	180 + 177 1771	2530 * TTC A(
08	* CTG	2430 * CGG	2480 * GCC TCT A S	* AAT
2380	CAC	* 00 0	¢ CTG	CIG
	* 99 o	ე	70 * CCT	2520 * ; GCC
	ATC	2420 * GGT GGG	2470 * CTG CC	000 000
2370	* ບ ິດ	2, GGT	* CAC	95 9
	* CTG	* CTG L	S	\$10 * AGC S
	E CAC	2410 * GCG GCG A A	2460 * CTC L	25 TCC AGC S S
2360	ACC T		A R	
2	CCC GAC P D	ATG M	CCT	2500 * CTG GGC L G
	* 000	GAG A	450 * CCA P	2500 * CTG G

FIG. 10M

00	- k	ည	Ġ	640	*	9	Ġ			SCC	Ÿ		*	TAC	\$
2590		AGC	တ		*	S S	Ф		*	ည္ပ	U			AGC	
		CAG				3	K				>	2730	*	ATG	Σ
		CIG		530	*	GTG	>	2680		ATG	Σ		*	ATG ATG	Σ
580	*	550 5	CC.	2630		AGT	ဟ		- k	ည္ဟ	U			CAG	a
(4	ŧ	TCC	ഗ			999				CAT	Ħ	2720	*	ICC	ഗ
		T.G	H	0	- *	950	ĸ	670	*	G CAG	a	27		CTG	ы
970	*	TGG	E E	2620		CTG	1		- *	CTG	ы		*	ည္ဟ	K
25		GAG	[L]		*	CCT	ሷ			TCC		2	*	AGC	ഗ
	*	795	ບຼ			AAC	z	960	*	ညည	A	27.1		ည္ဟ	X
20	*	B	a	2610	*	TAC	>	2(*	GCT	æ
2560		GGT	ဗ		*	CAA	a		*	CAG	a			CIT	니
	*	AAT	T S L			CCG AAC	z	20	*	CTG AGC ACA	Ħ	2700	*	CAC AGT AGC CTT	ഗ
		ITG	H	2600	-k	SSS	ᇝ	2650		AGC	ഗ		*	AGT	ഗ
2550	*	AGT	တ	7(ATG GTG	>		*	CIG	IJ			CAC	エ
. •	* r	ACC	E		*	ATG	Σ			ညည	വ	2690	*	CIG	니

FIG. 10N

	GRG 0	65 75 75 75 75	2880 CCA PV	87	* 5	5	
80	* GTG >	283 AAC N	* 67 9	CAC H	CAG	Ø	
2780	CIG	* CAG	5 0 a	ပ္ပံ ဗ ဝ * ဗ	2970 * GTG	> .	
	CAC H	CAG	70 CCG	292 AGC (GAC GAC	۵	FIG. 10 0
0	* CCT	2820 * CAG	2870 * CAG CCG	* 0 K	ţ	4	
277	CAG CC	A TG	CIG L	ઈ ∢	960 * CAG	a	
	* FCC	CAG	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	2910 * TCA (29. AGC (S	
	200 A	10 113 113	2860 CAA A(S S S	* 500	۵ ۵	
2760	crg .	28 AAC	* \$5 0	GTG	50 * GAG	ات ح	
	* 00 K	* & o	CAG		29 GGA	U L	-
	ACC	00 + OO PA	2850 * CAG	2900 * CTT GGC	* AGT	v	
2750	AGC S	2800 * CAG C	, AHOH	CAC H	CTG	ы	
	ည	* GTG (840 * GCA AAC 7 A N	2890 * CAG CCG Q P	2940 *	দি	
4	CIG (80	2840 * 'A GCA	N go	* * &	ဟ	
40	CAG GGC Q G	2790 * * ACC CAG	2 2 4 4 4	* Ω ч	9 90	ĸ	
2740	CAG	* AC	CAG	CCA	2930 * GGC	ڻ ا	

		AGC S>	o *	ACC 42	3120	CCT
3020	*	CAG GAG	3070	GTG	(·) +	TCG CCT
		CAG O	*	CCC		TCC
	*	CCC		C P P	110	TAC
0	*	CTG	3060	GIC	3110	AGC
3010		NC ACT ATT CT	*	CTG	+ x	CAC H
	*	ACT		TCG	0 *	Sko O
		CAC)50 *	CCA TCC P S	3100	TCG
3000	*	GTG V	3(T P	*	CCC P
` '	*	90g	*	CIG		CCC P
		CIG	O*	TCG	3090	ACG C
2990	*	AGC S	3040	CCC ACG	*	CIG
2		AGC S	*	CCC P		TTC
	*	Ω_{Ω}^{O}		CIG	3080	CAG
000	*	CTG GGC CCC AGC AGC L G P S S	3030	900 P	3(GCA GCC CAG TTC CTG A A Q F L
2980		CIG	*·	CCC GCC CTG (P A L	*	GCA

FIG. 10P

3160 GTT CCT V P 3210 * * * TCA ATT S I * CCT 3150 * CAG GTG Q V 3200 * AAA GGC K G cra cra rcr s 3140 * AGC CAC CAG (* B Q 3190 * * * * * CCT (3130 *
AAC ACC CCC N T P
3180 *
ATC CGA TCT I R
I R S
3230 *
CCC GAC TCA P GTG GAC V D 3170 * GTA ATG 1 V M 3220 GAA GCT C

FIG. 100

46								GAT (Asp \					
94	G AGT u Ser O				Gly				ı Alı				
142	A GAC Asp	Thr				Ser				ı Asp			
190	GGT		Arg				Gln				Gln		
238	GCC Ala												
286	ATG Met 95							Gly					
334								GCT Ala					
382	ATG Met							AAC Asn					
430								CTG Leu					

FIG.11A

	Val					GCG Ala			478
Asp						GCA Ala 170			526
						GGG Gly			574
						CTT Leu	Ala		622
						CAT His			670
						GAT Asp			718
						GAA Glu 250		_	766
		Gly				CTC Leu			814
						CAC His			862

FIG.11B

							•	7070	0							
						GCC Ala										910
						AAG Lys 310										958
TCT Ser 320	CTG Leu	AGT Ser	GAG Glu	AAG Lys	GTC Val 325	CAA Gln	CTG Leu	TCT Ser	GAG Glu	AGT Ser 330	TCA Ser	GTA Val	ACT Thr	TTA Leu	TCC Ser 335	1006
						TCT Ser										1054
						TCC Ser										1102
						GCC Ala										1150
						CTT Leu 390										1198
						TCA Ser										1246
ATT I le	GTG Val	TCT Ser	CCA Pro	GGC Gly 420	AGT Ser	GGC Gly	AGT Ser	GCT Ala	GGA Gly 425	AGC Ser	TTG Leu	AGT Ser	AGG Arg	CTC Leu 430	CAT His	1294
CCA Pro	GTC Val	CCA Pro	GTC Val 435	CCA Pro	GCA Ala	GAT Asp	TGG Trp	ATG Met 440	AAC Asn	CGC Arg	ATG Met	GAG Glu	GTG Val 445	AAT Asn	GAG Glu	1342

FIG.11C

37/68 ACC CAG TAC AAT GAG ATG TTT GGT ATG GTC CTG GCT CCA GCT GAG GGC Thr Gln Tyr Asn Glu Met Phe Gly Met Val Leu Ala Pro Ala Glu Gly 450 ACC CAT CCT GGC ATA GCT CCC CAG AGC AGG CCA CCT GAA GGG AAG CAC Thr His Pro Gly Ile Ala Pro Gln Ser Arg Pro Pro Glu Gly Lys His 465 470 ATA ACC ACC CCT CGG GAG CCC TTG CCC CCC ATT GTG ACT TTC CAG CTC 1486 Ile Ihr Thr Pro Arg Glu Pro Leu Pro Pro Ile Val Thr Phe Gln Leu 480 485 490 ATC CCT AAA GGC AGT ATT GCC CAA CCA GCG GGG GCT CCC CAG CCT CAG Ile Pro Lys Gly Ser Ile Ala Gln Pro Ala Gly Ala Pro Gln Pro Gln 500 505 510 TCC ACC TGC CCT CCA GCT GTT GCG GGC CCC CTG CCC ACC ATG TAC CAG Ser Thr Cys Pro Pro Ala Val Ala Gly Pro Leu Pro Thr Met Tyr Gln 515 520 525 ATT CCA GAA ATG GCC CGT TTG CCC AGT GTG GCT TTC CCC ACT GCC ATG Ile Pro Glu Met Ala Arg Leu Pro Ser Val Ala Phe Pro Thr Ala Met 530 535 540 ATG CCC CAG CAG GAC GGG CAG GTA GCT CAG ACC ATT CTC CCA GCC TAT Met Pro Gin Gin Asp Gly Gin Val Ala Gin Thr Ile Leu Pro Ala Tyr 545 550 555 CAT CCT TTC CCA GCC TCT GTG GGC AAG TAC CCC ACA CCC CCT TCA CAG His Pro Phe Pro Ala Ser Val Gly Lys Tyr Pro Thr Pro Pro Ser Gln 560 565 570 575 CAC AGT TAT GCT TCC TCA AAT GCT GCT GAG CGA ACA CCC AGT CAC AGT His Ser Tyr Ala Ser Ser Asn Ala Ala Glu Arg Thr Pro Ser His Ser 580 585 590 GGT CAC CTC CAG GGT GAG CAT CCC TAC CTG ACA CCA TCC CCA GAG TCT Gly His Leu Gln Gly Glu His Pro Tyr Leu Thr Pro Ser Pro Glu Ser 595

FIG.11D

600

605

WO 94/07474 PCT/US93/09338

38/68 CCT GAC CAG TGG TCA AGT TCA TCA CCC CAC TCT GCT TCT GAC TGG TCA 1870 Pro Asp Gln Trp Ser Ser Ser Ser Pro His Ser Ala Ser Asp Trp Ser 620 615 610 GAT GTG ACC ACC AGC CCT ACC CCT GGG GGT GCT GGA GGA GGT CAG CGG 1918 ASD Val Thr Thr Ser Pro Thr Pro Gly Gly Ala Gly Gly Gly Gln Arg 625 630 GGA CCT GGG ACA CAC ATG TCT GAG CCA CCA CAC AAC AAC ATG CAG GTT 1966 Gly Pro Gly Thr His Met Ser Glu Pro Pro His Asn Asn Met Gln Val 650 640 645 TAT GCG TGAGAGAGTC CACCTCCAGT GTAGAGACAT AACTGACTTT TGTAAATGCT 5055 Tyr Ala GCTGAGGAAC AAATGAAGGT CATCCGGGAG AGAAATGAAG AAATCTCTGG AGCCAGCTTC 2082 TAGAGGTAGG AAAGAGAAGA TGTTCTTATT CAGATAATGC AAGAGAAGCA ATTCGTCAGT 2142 TTCACTGGGT ATCTGCAAGG CTTATTGATT ATTCTAATCT AATAAGACAA GTTTGTGGAA 2202 ATGCAAGATG AATACAAGCC ITGGGTCCAT GTTTACTCTC TICTATITGG AGAATAAGAT 5565 GGATGCTTAT TGAAGCCCAG ACATTCTTGC AGCTTGGACT GCATTTTAAG CCCTGCAGGC 5355 TTCTGCCATA TCCATGAGAA GATTCTACAC TAGCGTCCTG TTGGGAATTA TGCCCTGGAA 5385 TICTGCCTGA ATTGACCTAC GCATCTCCTC CTCCTTGGAC ATTCTTTTGT CTTCATTTGG 2442 TGCTTTTGGT TTTGCACCTC TCCGTGATTG TAGCCCTACC AGCATGTTAT AGGGCAAGAC 2502 CTTTGTGCTT TTGATCATTC TGGCCCATGA AAGCAACTTT GGTCTCCTTT CCCCTCCTGT 2562 CTTCCCGGTA TCCCTTGGAG TCTCACAAGG TTTACTTTGG TATGGTTCTC AGCACAAACC 2622 TTTCAAGTAT GTTGTTTCTT TGGAAAATGG ACATACTGTA TTGTGTTCTC CTGCATATAT 2682 CATTCCTGGA GAGAGAAGGG GAGAAGAATA CITTTCTTCA ACAAATTTTG GGGGCAGGAG 2742 ATCCCTTCAA GAGGCTGCAC CTTAATTITT CTTGTCTGTG TGCAGGTCTT CATATAAACT 5805

FIG.11E

SUBSTITUTE SHEET (RULE 26)

TTACCAGGAA GAAGGGTGTG AGTTTGTTGT TTTTCTGTGT ATGGGCCTGG TCAGTGTAAA	2868
GTTTTATCCT TGATAGTCTA GTTACTATGA CCCTCCCCAC TTTTTTAAAA CCAGAAAAAG	2922
GTTTGGAATG TTGGAATGAC CAAGAGACAA GTTAACTCGT GCAAGAGCCA GTTACCCACC	2982
CACAGGTCCC CCTACTTCCT GCCAAGCATT CCATTGACTG CCTGTATGGA ACACATTTGT	3042
CCCAGATCTG AGCATTCTAG GCCTGTTTCA CTCACTCACC CAGCATATGA AACTAGTCTT	3102
AACTGTTGAG CCTTTCCTTT CATATCCACA GAAGACACTG TCTCAAATGT TGTACCCTTG	3162
CCATTTAGGA CTGAACTTTC CTTAGCCCAA GGGACCCAGT GACAGTTGTC TTCCGTTTGT	3555
CAGATGATCA GTCTCTACTG ATTATCTTGC TGCTTAAAGG CCTGCTCACC AATCTTTCTT	3282
TCACACCGTG TGGTCCGTGT TACTGGTATA CCCAGTATGT TCTCACTGAA GACATGGACT	3342
TTATATGTTC AAGTGCAGGA ATTGGAAAGT TGGACTTGTT TTCTATGATC CAAAACAGCC	3402
CTATAAGAAG GTTGGAAAAG GAGGAACTAT ATAGCAGCCT TTGCTATTTT CTGCTACCAT	3462
TICTITICCI CIGAAGCGGC CATGACATIC CCTTIGGCAA CTAACGTAGA AACTCAACAG	3522

FIG.11F

WO 94/07474 PCT/US93/09338

40/68

AACATTITCC TITCCTAGAG TCACCTITTA GATGATAATG GACAACTATA GACTTGCTCA 3582 TTGTTCAGAC TGATTGCCCC TCACCTGAAT CCACTCTCTG TATTCATGCT CTTGGCAATT 3642 TCTTTGACTT TCTTTTAAGG GCAGAAGCAT TTTAGTTAAT TGTAGATAAA GAATAGTTTT 3702 CTTCCTCTTC TCCTTGGGCC AGTTAATAAT TGGTCCATGG CTACACTGCA ACTTCCGTCC 3762 AGTGCTGTGA TGCCCATGAC ACCTGCAAAA TAAGTTCTGC CTGGGCATTT TGTAGATATT 3822 AACAGGTGAA TTCCCGACTC TTTTGGTTTG AATGACAGTT CTCATTCCTT CTATGGCTGC 3882 AAGTATGCAT CAGTGCTTCC CACTTACCTG ATTTGTCTGT CGGTGGCCCC ATATGGAAAC 3942 CCTGCGTGTC TGTTGGCATA ATAGTTTACA AATGGTTTTT TCAGTCCTAT CCAAATTTAT 4002 TGAACCAACA AAAATAATTA CTTCTGCCCT GAGATAAGCA GATTAAGTTT GTTCATTCTC 4062 TGCTTTATTC TCTCCATGTG GCAACATTCT GTCAGCCTCT TTCATAGTGT GCAAACATTT 4122 TATCATTCTA AATGGTGACT CTCTGCCCTT GGACCCATTT ATTATTCACA GATGGGGAGA 4182 ACCTATCTGC ATGGACCCTC ACCATCCTCT GTGCAGCACA CACAGTGCAG GGAGCCAGTG 4242 GCGATGGCGA TGACTTTCTT CCCCTG 4268

FIG. 11G

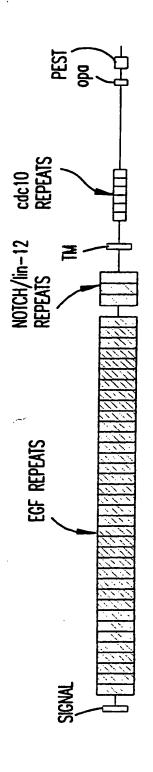
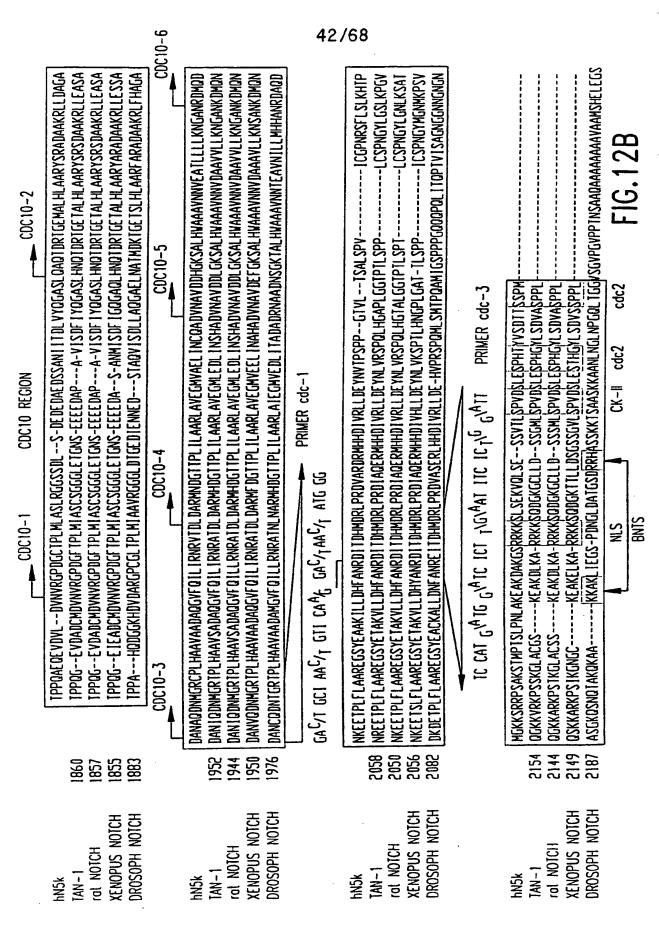


FIG. 12A



SUBSTITUTE SHEET (RULE 26)

43/00	4	3	/	6	8
-------	---	---	---	---	---

PVGVGMGGNL PSPYBISSMYSNAMAAPLANGNPN1GAKQPRSYEDC I KNAQSMQSLQGNGL DM1KL DNYAYSMGSPRDQSPSMPL HILL 1 SMPESQLGMNH1NMA CK-11	SNLHEMD	APOSRPPEGK
2218	2250	2354
2209	2242	2344
2214	2247	2343
2285	2390	2495
hNSk	hNSk	hNSk
IAN-1	TAN-1	TAN-1
rat NDICH	rat NDTCH	rat NDTCH
XENDPUS NDICH	XENDPUS NDTCH	XENGPUS NDTCH
. DRDSOPH NDICH	DROSOPH NOTCH	DROSGPH NDTCH
1_1_>	SUBSTITUTE SHI	EET (RULE 26)

PEST-CONTAINING REGION

S---10SSMSG-SSPSTNMLSPSSQHNQQAFYQYL|TPSSQHS-----GGHTPQHLVQTL-D-SYPTPSPESPGHVSSSSPRSN-SDVSEGVQSPAA

2423 2416 2599

> XENDPUS NOTCH DROSOPH NOTCH

hNSk TAN-1 rat NDICH

2448

SVAFPTAMMPQQDGQVAQTILPAYHPFPASVGKYHITPPSQHSYASSNAAERTPSHSGHLQGEHPYLTPSPESPDQVSSSSPHSA-SDVSDVTTSPTP

SSLAVHTILPO-ESPALPTSLPSSLVPPVTAAOFLİTPPSOHSY-SS-PVENTPSHOLOVP-EHPFLTPSPESPDOWSSSSPHSNVSDWSEGVSSPPT SSLPVHT ILPO-ESQALPTSLPSSMVPPMTTTOFL|TPPSQHSY-SSSPVDNTPSHOLQVP-EHPFLTPSPESPDQWSSSSRHSNI SDWSEGISSPPT SSNN I HSVMPQ-DTQIF AASLPSNL TQSMTTAQFL|TPPSQHSY-SS-PMDNTPSHQLQVP-DHPFL TPSPESPDQVSSSSPHSNMSDVSEGISSPPT

FIG. 12C

			Potenti	al signal c	leavage sit	e	Ì
hum N	MP		——AI RPAI	I WAI LALWLC	CAAPA	HA	•
TAN-1						RGP	
Xen N	MD			RIGLAVLLCS	LPVLT	QCL	
Dros N		RAPNTWICFW	INKMHAVASL	PASLPLLLLT	LAFANLPNIV	RGTDTAL VA'A	.
hum N						CQVGFTGKEC	
Tan-1						CPPGWSGKSC	>
Xen N						CPPGWTGDSC	1
Dros N	GRPG1SCKCP	LGFDESLCE I	AVPNAC-DHV	TCLNGGTCQL	KT-LEEYTCA	CANGYTGERC	.
	NLPGSYQCQC						
	: NEVGSYRCVC						
	· NEFGSYRCTC						
Dros N	NTHGSYQCMC	PTGYTGKDCD	TKYNPCSPSP	CQNAG I CRSN	G-LSYECKCP	KGFEGKNCEQ	l
			. 	·)
	EGF-like R	epeats					J
	QCRDGYEPCV	NEGMCVTYHN				GGTCVAQA	ر 83
	QCRDGYEPCV RCSQPGETCL	NEGMCVTYHN NGGKCEA-AN	GTEACVCGGA	FVGPRCQDPN	PCL-STPCKN	AGTCHVVDRR	80
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG	GTEACVCGGA GTGVCLCGNL	FVGPRCQDPN YFGERCQFPN	PCL-STPCKN PCT I KNQCMN	AGTCHVVDRR FGTCEPVLQG	80 90
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG	GTEACVCGGA GTGVCLCGNL	FVGPRCQDPN YFGERCQFPN	PCL-STPCKN PCT I KNQCMN	AGTCHVVDRR	80
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL SCTSVG—CQ	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG NGGTCVTQLN CANGSTCTTV	GTEACVCGGA GTGVCLCGNL GKTYCACDSH —ANQFSCKC	FVGPRCQDPN YFGERCQFPN YVGDYCEHRN LTGFTGQKCE	PCL-STPCKN PCT1KNQCMN PCN-SMRCQN TDVNEC-DIP	AGTCHVVDRR FGTCEPVLQG GGTCQVTFRN GHCQHGGTCL	80 90 117 199
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL SCTSVG—CQ QWTDACLSHP QQADPCASNP	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG NGGTCVTQLN CANGSTCTTV CANGGQCLPF	GTEACVCGGA GTGVCLCGNL GKTYCACDSH —ANQFSCKC —EASYICHC	FVGPRCQDPN YFGERCQFPN YVGDYCEHRN LTGFTGQKCE PPSFHGPTCR	PCL-STPCKN PCTIKNQCMN PCN-SMRCQN TDVNEC-DIP QDVNECGQKP	AGTCHVVDRR FGTCEPVLQG GGTCQVTFRN GHCQHGGTCL RLCRHGGTCH	80 90 117 199 196
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL SCTSVG—CQ QWTDACLSHP QQADPCASNP QQADPCASNP	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG NGGTCVTQLN CANGSTCTTV CANGGCLPF CANGGKCLPF	GTEACVCGGA GTGVCLCGNL GKTYCACDSH —ANQFSCKC —EASYICHC —EIQYICKC	FVGPRCQDPN YFGERCQFPN YVGDYCEHRN LTGFTGQKCE PPSFHGPTCR PPGFHGATCK	PCL-STPCKN PCT1KNQCMN PCN-SMRCQN TDVNEC-DIP QDVNECGQKP QDINEC-S-Q	AGTCHVVDRR FGTCEPVLQG GGTCQVTFRN GHCQHGGTCL RLCRHGGTCH NPCKNGGQCI	80 90 117 199 196 195
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL SCTSVG—CQ QWTDACLSHP QQADPCASNP QQADPCASNP	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG NGGTCVTQLN CANGSTCTTV CANGGCLPF CANGGKCLPF	GTEACVCGGA GTGVCLCGNL GKTYCACDSH —ANQFSCKC —EASYICHC —EIQYICKC	FVGPRCQDPN YFGERCQFPN YVGDYCEHRN LTGFTGQKCE PPSFHGPTCR PPGFHGATCK	PCL-STPCKN PCTIKNQCMN PCN-SMRCQN TDVNEC-DIP QDVNECGQKP	AGTCHVVDRR FGTCEPVLQG GGTCQVTFRN GHCQHGGTCL RLCRHGGTCH NPCKNGGQCI	80 90 117 199 196
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL SCTSVG—CQ QWTDACLSHP QQADPCASNP QQADPCASNP ETKNLCASSP	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG NGGTCVTQLN CANGSTCTTV CANGGQCLPF CANGGKCLPF CRNGATCTAL	GTEACVCGGA GTGVCLCGNL GKTYCACDSH —ANQFSCKC —EASYICHC —EIQYICKC AGSSSFTCSC NTYNCRCPPQ	FVGPRCQDPN YFGERCQFPN YVGDYCEHRN LTGFTGQKCE PPSFHGPTCR PPGFHGATCK PPGFTGDTCS WTGQFCTEDV	PCL-STPCKN PCT1KNQCMN PCN-SMRCQN TDVNEC-DIP QDVNECGQKP QD1NEC-S-Q YD1EEC-Q-S DECLLQPNA-	AGTCHVVDRR FGTCEPVLQG GGTCQVTFRN GHCQHGGTCL RLCRHGGTCH NPCKNGGQCI NPCKYGGICV CQNGGTCANR	80 90 117 199 196 195 233 318
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL SCTSVG—CQ QWTDACLSHP QQADPCASNP QQADPCASNP ETKNLCASSP NIDDCPNHRC NIDDCPGNNC	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG NGGTCVTQLN CANGSTCTTV CANGGQCLPF CANGGKCLPF CRNGATCTAL QNGGVCVDGV KNGGACVDGV	GTEACVCGGA GTGVCLCGNL GKTYCACDSH —ANQFSCKC —EASYICHC —EIQYICKC AGSSSFTCSC NTYNCRCPPQ NTYNCPCPPE	FVGPRCQDPN YFGERCQFPN YVGDYCEHRN LTGFTGQKCE PPSFHGPTCR PPGFHGATCK PPGFTGDTCS WTGQFCTEDV WTGQYCTEDV	PCL-STPCKN PCT1KNQCMN PCN-SMRCQN TDVNEC-DIP QDVNECGQKP QD1NEC-S-Q YD1EEC-Q-S DECLLQPNA- DECQLMPNA-	AGTCHVVDRR FGTCEPVLQG GGTCQVTFRN GHCQHGGTCL RLCRHGGTCH NPCKNGGQC1 NPCKYGG1CV CQNGGTCANR CQNGGTCHNT	80 90 117 199 196 195 233 318 315
	QCRDGYEPCV RCSQPGETCL RCTQTAEMCL SCTSVG—CQ QWTDACLSHP QQADPCASNP QQADPCASNP ETKNLCASSP NIDDCPNHRC NIDDCPSNNC	NEGMCVTYHN NGGKCEA-AN NGGRCEMTPG NGGTCVTQLN CANGSTCTTV CANGGCLPF CANGGKCLPF CRNGATCTAL ONGGVCVDGV KNGGACVDGV RNGGTCVDGV	GTEACVCGGA GTGVCLCGNL GKTYCACDSH ANQFSCKCEASYICHCEIQYICKC AGSSSFTCSC NTYNCRCPPQ NTYNCPCPPE NTYNCQCPPD	FVGPRCQDPN YFGERCQFPN YVGDYCEHRN LTGFTGQKCE PPSFHGPTCR PPGFHGATCK PPGFTGDTCS WTGQFCTEDV WTGQYCTEDV WTGQYCTEDV	PCL-STPCKN PCT1KNQCMN PCN-SMRCQN TDVNEC-DIP QDVNECGQKP QD1NEC-S-Q YD1EEC-Q-S DECLLQPNA- DECQLMPNA-	AGTCHVVDRR FGTCEPVLQG GGTCQVTFRN GHCQHGGTCL RLCRHGGTCH NPCKNGGQCI NPCKYGGICV CQNGGTCANR CQNGGTCHNT CQNGGTCHNT	80 90 117 199 196 195 233 318

FIG.13A

hum N	NGGYGCVCVN	GWSGDDCSEN	IDDCAFASCT	PGSTCIDRVA	SFSCMCPEGK	AGLLCHLDDA
TAN-1	HCGYNCVCVN	GWTGEDCSEN	IDDCASAACF	HGATCHDRVA	SFYCECPHGR	TGLLCHLNDA
Xen N	YGGYNCVCVN	GWTGEDCSEN	IDDCANAACH	SCATCHDRVA	SFYCECPHGR	TGLLCHLDNA
Dros N	HGSYSCICVN	GWAGLDCSNN	TDDCKQAACF	YGATCIDGVG	SFYCQCTKGK	TGLLCHLDDA
hum N	AFHCECLKGY	AGPRCEMD IN	ECHSDPCQND	ATCLDK IGGF	TCLCMPGFKG	VHCELE INEC
TAN-1	SFECQCLQGY	TGPRCE I DVN	ECVSNPCQND	ATCLDQIGEF	QCMCMPGYEG	VHCEVNTDEC
Xen N	SFOCNCPOGY	AGPRCE IDVN	ECLSNPCOND	STCLDQIGEF	QCICMPGYEG	LYCETNIDEC
Dros N	SYRCNCSQGF	TGPRCETNIN	ECESHPCQNE	GSCLDDPGTF	RCVCMPGFTG	TOCEIDIDEC
hum N	ATGF TGVLCE	ENIDNCDPDP	CHHGQCQDG I	DSYTCICNPG	YMGAICSDQ1	DECYSSPCLN
TAN-1	TEGYTGTHCE	VDIDECOPDP	CHYGSCKDGV	ATFTCLCRPG	YTGHHCETNI	NECSSOPCRL
Xen N	TEGFTGRHCE	QDINECIPDP	CHYGTCKDGI	ATFTCLCRPG	YTGRLCDND1	NECLSKPCLN
Dros N	PPGYTGTSCE	ININDCDSNP	CHRGKCIDDV	NSFKCLCDPG	YTGYICQKQI	NECESNPCQF

01010011101						-
CISNPCHKGA	LCDINPLNGQ	YICTCPQGYK	GADCTEDVDE	CAMANSNPCE	HAGKCVNTDG	438
CISNPCNEGS	NCDTNPVNGK	AICTCPSGYT	GPACSQDVDE	CSLG-ANPCE	HAGKCINTLG	434
CISNPCNEGS	NCDTNPVNGK	AICTCPPGYT	GPACNNDVDE	CSLG-ANPCE	HGGRCTNTLG	433
CTSNPCHADA	ICDTSPINGS	YACSCATGYK	GVDCSEDIDE	CDQG-SPCE	HNG I CVNTPG	470
						-
QSNPCVNNGQ	CVDKVNRFQC	LCPPGF TGPV	COIDIDDCSS	TPCLNGAKC I	DHPNGYECQC	- 558
ASSPCLHNGR	CLDKINEFQC	ECPTGF TGHL	CQYDVDECAS	TPCKNGAKCL	DGPNTYTCVC	554
ASNPCLHNGK	CIDKINEFRC	DCPTGFSGNL	CQHDFDECTS	TPCKNGAKCL	DGPNSYTCQC	553
QSNPCLNDGT	CHDKINGFKC	SCALGF TGAR	CQINIDDCQS	QPCRNRG I CH	DSIAGYSCEC	. 590
						•
DGRCIDLVNG	YQCNCQPGTS	GVNCE I NFDD	CASNPC I HG-	ICMDG INRYS	CVCSPGF TGQ	677
RGTCQDPDNA	YLCFCLKGTT	GPNCEINLDD	CASSPCDSG-	TCLDK IDGYE	CACEPGYTGS	673
GGQCTDRENG	YICTCPKGTT	GVNCETKIDD	CASNLCDNG-	KCIDK IDGYE	CTCEPGYTCK	672
DGHCQDRVGS	YYCQCQAGTS	GKNCEVNVNE	CHSNPCNNGA	TCIDGINSYK	CQCVPGFTGQ	710

FIG.13B

hum, N	RCNIDIDECA SNPCRKGATC INGVNGFRCI CPEGPHHPSC YSQVNECLSN PCI-HGNCTG
TAN-1	MCNSNIDECA GNPCHNGGTC EDGINGFTCR CPEGYHDPTC LSEVNECNSN PCV-HGACRD
Xen N	LCNININECD SNPCRNGGTC KDQINGFTCV CPDGYHDHMC LSEVNECNSN PCI-HGACHD
Dros N	HCEKNVDECI SSPCANNGVC IDQVNGYKCE CPRGFYDAHC LSDVDECASN PCVNEGRCED
hum N	DECASNPCLN QCTCFDD1SG YTCHCVLPYT GKNCQTVLAP CSPNPCENAA VCKESPNFES
TAN-1	! NECASNPCLN KGTCIDDVAG YKCNCLLPYT GATCEVVLAP CAPSPCRNGG ECRQSEDYES
Xen N	NECSSNPCLN HGTCIDDVAG YKCNCMLPYT GAICEAVLAP CAGSPCKNGG RCKESEDFET
Dros N	DDCVTNPCGN GGTC1DKVNG YKCVCKVPFT GRDCESKMDP CASNRCKNEA KCTPSSNFLD
hum N	CLANPCONGG SCMDGVNTFS CLCLPGFTGD KCQTDNMECL SEPCKNGGTC SDYVNSYTCK
TAN-1	CRPNPCHNGG SCTDGINTAF CDCLPGFRGT FCEEDINECA SDPCRNGANC TDCVDSYTCT
Xen N	COPNPCHAGG SCSDGINAFF CACPAGERGP KCEEDINECA SAPCKAGANC TOCVASYTCT
Dros N	CASFPCONGG TOLDGIGDYS CLOVDGFDGK HOETDINECL SQPCONGATO SQYVNSYTOT

_							
	GLSGYKCLCD	AGWVG INCEV	DKNECLSNPC	QNGGTCDNLV	NGYRCTCKKG	FKGYNCQVNI	796
	SLNGYKCDCD	PGWSGTNCDI	NNNECESNPC	VNGGTCKDMT	SGIVCTCREG	FSGPNCQTNI	792
	GVNGYKCDCE	AGWSGSNCDI	NNNECESNPC	MNGGTCKDMT	GAYICTCKAG	FSGPNCQTNI	791
	GINEFICHCP	PGYTGKRCEL	DIDECSSNPC	QHGGTCYDKL	NAFSCQCMPG	YTGQKCETNI	830
	YTCLCA-PGW	QGQRCTIDID	EC-ISKPCMN	HGLCHNTQGS	YMCECPPGFS	GMDCEEDIDD	914
	FSCVCPTAGA	KGQTCEVDIN	EC-VLSPCRH	GASCQNTHGG	YRCHCQAGYS	GRNCETDIDD	911
	FSCECP-PGW	QGQTCE IDMN	EC-VNRPCRN	GATCONTNGS	YKCNCKPGYT	GRNCEMDIDD	909
	FSCTCK-LGY	TGRYCDEDID	ECSLSSPCRN	GASCLNVPGS	YRCLCTKGYE	GRDCAINTDD	949
	COAGFDGVHC	ENNINECTES	SCFNGGTCVD	GINSFSCLCP	VGFTGSFCLH	EINECSSHPC	1034
	CPAGFSG IHC	ENNTPDCTES	SCFNGGTCVD	GINSFTCLCP	PGFTGSYCQH	VVNECDSRPC"	1031
	COPGFSGIHC	ESNTPDCTES	SCFNGGTCID	GINTFTCQCP	PGFTGSYCQH	DINECDSKPC	1029
	CPLGFSG INC	QTNDEDCTES	SCLNGGSCID	GINGYNCSCL	AGYSGANCQY	KLNKCDSNPC	1069
							

FIG.13C

hum N	LNEGTCVDGL GTYRCSCPLG YTGKNCQTLV NLCSRSPCKN KGTCVQKKAE SQCLCPSGWA
TAN-1	LLGGTCQDGR GLHRCTCPQG YTGPNCQNLV HWCDSSPCKN GGKCWQTHTQ YRCECPSGWT
Xen N	LNGGTCQDSY GTYKCTCPQG YTGLNCQNLV RWCDSSPCKN GGKCWQTNNF YRCECKSGWT
Dros N	LNGATCHEON NEYTCHCPSG FTGKQCSEYV DWCGQSPCEN GATCSQMKHQ FSCKCSAGWT
hum N	SNPCQHGATC SDFIGGYRCE CVPGYQGVNC EYEVDECQNQ PCQNGGTCID LVNHFKCSCP
TAN-1	PSPCQNGATC TDYLGGYSCK CVAGYHGVNC SEEIDECLSH PCQNGGTCLD LPNTYKCSCP
Xen N	PNPCQNGATC TDYLGGYSCE CVAGYHGVNC SEEINECLSH PCQNGGTCID LINTYKCSCP
Dros N	SQPCQNGGTC RDLIGAYECQ CRQGFQGQNC ELNIDDCAPN PCQNGGTCHD RVMNFSCSCP
hum N	CLSNPCSSEG SLDCIQLTND YLCVCRSAFT GRHCETFVDV CPOMPCLNGG TCAVASNMPD
TAN-1	CLSNPCDARG TONCVORVND FHCECRAGHT GRRCESVING CKGKPCKNGG TCAVASNTAR
Xen N	CLSNPCDSRG TONCIQLVND YRCECROGFT GRRCESVVDG CKGMPCRNGG TCAVASNTER
Dros N	CLSNPCSNAG TLDCVQLVNN YHCNCRPGHM GRHCEHKVDF CAQSPCQNGG NCNI-RQS

```
GAYCDVPNVS CDIAASRRGV LVEHLCQHSG VCINAGNTHY CQCPLGYTGS YCEEQLDECA 1154
GLYCDVPSVS CEVAAQRQGV DVARLCQHGG LCVDAGNTHH CRCQAGYTGS YCEDLVDECS 1151
GVYCDVPSVS CEVAAKQQGV DIVHLCRNSG MCVDTGNTHF CRCQAGYTGS YCEEQVDECS
GKLCDVQTIS CQDAADRKGL SLRQLC-NNG TCKDYGNSHV CYCSQGYAGS YCQKEIDECQ
PGTRGLLCEE NIDDCAR --- GPHCLN GGOCMDRIGG YSCRCLPGFA GERCEGDINE 1267
RGTQGVHCEI NVDDCNPPVD PVSRSPKCFN NGTCVDQVGG YSCTCPPGFV GERCEGDVNE
                                                                  1271
RGTQGVHCEI NVDDCTPFYD SFTLEPKCFN NGKCIDRVGG YNCICPPGFV GERCEGDVNE
                                                                  1269
PGTMGIICEI NKDDCKP----
                          -GACHN NGSCIDRVGG FECVCQPGFV GARCEGDINE
                                                                  1300
GFICRCPPGF SGARCOS—— SCGQVKCRKG EQCVHTAS—— GPRCFCPSP——RDCES—
                                                                  1376
GFICKCPAGF EGATCENDAR TCGSLRCLNG GTCISGPR- SPTCLCLGPF TGPECQFPAS
                                                                  1389
GFICKCPPGF DGATCEYDSR TCSNLRCQNG GTCISVLT- SSKCVCSEGY TGATCQYPVI
                                                                  1387
GHHCICNNGF YGKNCELSGQ DCDSNPCRVG -NCVVADEGF GYRCECPRGT LGEHCEIDTL
                                                                  1415
```

FIG. 13D

hum N	-GC-ASSPCQ HGGSCHPQRQ PPYYSCOCAP PFSGSRCELYTAPP
TAN-1	SPCLGGNPCY NOGTCEPTSE SPFYRCLCPA KFNGLLCHIL DYSFGG
Xen N	SPC-ASHPCY NGGTCOFFAE EPFFOCFCPK NFNGLFCHIL DYEFPG
Dros N	DEC-SPNPCA OGAACEDLLG D-YECLCPS KWKGKRCDIY DANYPGWNGG SGSGNDRYAA
hum N	NN-QCDELCN TVECLFDNFE CQGNSKTCKYDKYCADHF KDNHCNQGCN SEECGWDGLD
TAN-1	SDGHCDSQCN SAGCLFDGFD CQRAEGQCNP LYDQYCKDHF SDGHCDQGCN SAECEWDGLD
Xen N	NDGKCDSQCN NTGCLYDGFD CQKVEVQCNP LYDQYCKDHF QDGHCDQGCN NAECEWDGLD
Dros N	KNGKCNEECN NAACHYDGHD CERKLKSCDS LFDAYCQKHY GDGFCDYGCN NAECSWDGLD
hum N	YYGEKSAAMK KQ—R——————————————————————————————————
TAN-1	YYGREELRK HPIKRAAEGW AAPDALLGQV KASLLPGGSE GGRRRRELDP MDVRGSIVYL
Xen N	YYGNEEELKK HHIKRSTDYW SDAPSAI FSTMKESIL LGRHRRELDE MEVRGSIVYL
Dros N	WKDNVRVPEI EDTDFARKNK ILYTQQVHQ TGIQIYL
	•
1	
1	LNR (Notch/Lin-12 Repeats)
ļ	Link (notchy Lini-12 Nepeuts)

-	7						_
	ATCL	SQYCADKARD	GVCDEACNSH	ACOWDGGDCS	LTMENPWANC	SSPLPCWDYI	1476
	LIEE—ACE	LPECQEDAGN	KVCSLQCNNH	ACGWDGGDCS	LNFNDPWKNC	TOSLOCWKYF	1501
	DNDDICE	NEQCSELADN	KVCNANCNNH	ACGWDGGDCS	LNFNDPWKNC	TOSL OCWKYF	1498
	DLEQQRAMCD	KRGCTEKQGN	GICDSDCNTY	ACNFDGNDCS	LGI-NPWANC	TAN-EXWNKF	1531
l				· · · · · · · · · · · · · · · · · · ·			
l	CA'ADQPEN-L	AEGTLVIVVL	MPPEQLLQDA	R-SFLRALGT	LLHTNLRIKR	DSQGELMVYP	1591
	CAEHVPER-L	AAGTL-VVVV	LMPPEQLRNS	SFHFLRELSR	VLHTNVVFKR	DAHGOOMIFP	1619
,	C-:ANMPEN-L	AEGTLVLVVL	MPPERLKNNS	V-NFLRELSR	VLHTNVVFKK	DSKGFYKTYP	1615
l	CENKTQSPVL	AEGAMSVVML	MNVEAFREIQ	A-QFLRNMSH	MLRTTVRLKK	DALGHDIIIN	1650
						TM	
	EIDNRQCVQD	SDHCFKNTDA	AAALLASHAI	QGTLSYP	LVSVVSESLT	PERT-O-IIY	1680
	EIDNRQCVQA	SSQCFQSATD	VAAFLGALAS	LGSL-NIPYK	IEAVOSETVE	PPPPAO-I HF	1737
	EIDNRQCYKS	SSQCFNSATD	VAAFLGALAS	LGSLDTLSYK	IEAVKSENM F	TPKPST-I YP	1730
	EIDNRKCTEC	FTHAVEAAEF	LAATAAKHOL	RNDFQ-IHSV	RGIKNPGDED	NGFPPANVKY	1745
`	•					MOLI I MINT	1743

FIG.13E

hum N	LLAVAVVIIL FIILLGVIMA KRKRK-HGS LWLPEGFTLR RDASNHKRRE PVGQDAVG	a K
TAN-1	MYVAAAAFVL LFFVGCGVLL SRKRRRQHGQ LWFPEGFKV- SEASKKKRRE ELGEDSVG	I K
Xen N	MLSMLVIPLL IIFVFMMVIV NKKRRREHDS FGSPTALFOK NPA-KRNGET PW-EDSVG	l K
Dros N	VITCIILVII ALAFFOMVL- STORKRAHOV TWFPEGFRAP AAVMSRRRD PHODEMRN	I N
	CDC-10/Ankyrin Repea	
hum N	PIDRRPWTQQ HLEAADIRRT PSLALTPPQA EQEVDVLDVN VRGPDGCTPL MLASLRGG	SS
TAN-1	QTDHRQWTQQ HLDAADL-RM SAMAPTPPQG EVDADCMDVN VRGPDGFTPL MIASCSGG	GL
Xen N	KTDPROWTRQ HLDAADL-RI SSMAPTPPQG EIEADCMDVN VRGPDGFTPL MIASCSGG	GL
Dros N	EADQRVWSQA HLDVVDV-R- AIMTPP-A HQDGGKHDVD ARGPCGLTPL MIAAVRGGC	3L
hum N	ANAQDNMGRC PLHAAVAADA QGVFQILIRN RVTDLDARMN DGTTPLILAA RLAVEGMVA	λ <u>E</u>
TAN-1	ANIQDNMGRT PLHAAVSADA QGVFQILIRN RATDLDARMH DGTTPLILAA RLAVEGMLF	D
Xen N	ANVODNINGRI PLHAAVAADA QGVFQILIRN RATDLDARNF DGTTPLILAA RLAVEGMVE	F
Dros N	ANCODNIGRI PLHAAVAADA MGVFQILLRN RAINLNARMH DGIIPLILAA RLAIEGMVE	D
		ニン

```
NLSVQVSEAN LIGTGTSEHW VDDE-------G PQPKKVKAED EALLSE-EDD
                                                             1782
1837
                                                             1831
KQVAMQSQCV GQPGAH---W SDDESDMPLP KRQRSDPVSG VGLGNNGGYA SDHTMVSEYE
                                                             1861
DLSDEDEDAE DSSANIITDL VYQGASLQAQ TDRTGEMALH LAARYSRADA AKRLLDAGAD
                                                             1902
ETGNSEEE-E DAPA-VISDF IYQGASLHNQ TDRTGETALH LAARYSRSDA AKRLLEASAD
                                                             1954
ETGNSEEE-E DASANMISDF IGQGAQLHNQ TDRTGETALH LAARYARADA AKRLLESSAD
                                                             1949
DTGEDIENNE DSTAQVISDL LAQGAELNAT MDKTGETSLH LAARFARADA AKRLLDAGAD
                                                             1976
LINCQADVNA VDDHGKSALH WAAAVNNVEA TLLLLKNGAN RDMQDNKEET PLFLAAREGS
                                                             2022
LINSHADVNA VDDLGKSALH WAAAVNNVDA AVVLLKNGAN KDMQNNREET PLFLAAREGS
                                                             2074
LINAHADVNA VDEFGKSALH WAAAVNNVDA AAVLLKNSAN KDMQNNKEET SLFLAAREGS
                                                            2069
LITADADINA ADNSGKTALH WAAAVNNTEA VNILLMHAN RDAQDDKDET PLFLAAREGS
                                                            2096
```

FIG. 13F

							1
hum N	YEAAKILLDH	FANRDITDHM	DRLPRDVARD	RMHHDIVRLL	DEYNVTPSPP	-GTVL-TS	
				RMHHDIVRLL			
Xen N	YETAKVLLDH	YANRD I TOHM	DRLPRDIAGE	RMHHDIVHLL	DEYNLVKSPT	LHNGPLGAT-	
Dros N	YEACKALLDN	FANRE I TOHM	DRLPRDVASE	RLHHDIVRLL	DE-HVPRSPQ	MLSMTPQAMI	
	NLS		CK II	cdc2	cdc2		
hum N	GSRRKKSLSE	KVQLSE—SS	VTLSPVDSLE	SPHTYVSDTT	SSPM		
TAN-1	A-RRKKSQDG	KGCLLD-SS	GMLSPVDSLE	ISPHCYLSDVA	ISPPL		
Xen N	A-RRKKSQDG	KTTLLDSGSS	GVLSPVD SLE	ISTHCYLSDVS	ISPPL		
Dros N	GS-PDNGLDA	TGSLIRRKASS	KKTSAASKKA	ANLNGLNPGQ	LTGGVSGVPG	VPPTNSAAQA	
	BNTS						
hum N				ITSPGIL <u>OA</u> S	PNPML-ATA	APPAPVHAQH	
TAN-1				LPSPFQQS			
Xen N				MTSPF-QQS	PSMPLNHLTS	MPESQLGMNH	
Dros N	YEDCIKNAQS	MQSLQGNGLD	MIKLDNYAYS	MGSPF-QQE	LENGQGLGMN	GNGQRNGVGP	i
	CK II			cdc2			ノ
	AI SPV	ICCP	NRSEI SI KHT	PMCKKSRRPS	AKSTMPTSI P	NI AKFAKDAK	2127
				VQCKKVRKPS			2178
						KEAKELK	2170
		-				KKAKL IE	
Ì							
ļ .							2169
J							2219
							2213
1			OUDLIOONII DC	DVINTCCLAVCKI	AMA ADI AMPNI	DAITC AVODDC:	2327
	AAAAAAAA	MSHELEGSPV	GVGMGGNLPS	LIN122W12M	AWAAFLANGIN	PINIUANUPPS.	2321
	AAAAAAAVAA						
	ALSFSNLHEM					HHIVSPGS—	

FIG.13G

LNVAA-KPEM AALGGGGRLA FETGPPRLSH LPVASGTSTV LGSSSGGALN FTVGGSTSLN 2306 INMAT-KQEM AA-GSNRMA FDAMVPRLTH L-NASSPNTI MS---NGSMH FTVGGAPTMN 2294 GVLPGGLCGM GGLSGAGNGN SHEQGLSPPY SNQSPPHSVQ SSLALSPHAY LGSPSPAKSR 2445

hum N	GSAGSLSRLH PVPVPADW— MNRMEVNETQ YNEMFGMVLA PAEG-THPGI APOSRPPEGK
TAN-1	GQCEWLSRLQ SGMVPNQYNP LRGSVAPGPL STQAPSLQHG -MVGPLHSSL AASALSQMMS
Xen N	SQCDWLARLQ NGMVQNQYDP IRNGIQQGN- AQQAQALQHG LMTS-LHNGL PATTLSQAMT
Dros N	PSLPTSPTHI QAMRHATQQK QFGGSNLNSL LGGANGGGVV GGGGGGGGGV GQCPQNSPVS
hum N	APQPQSTCPP AVAGPLPTMY QIPEM ARL-PSVAFP TAMMPQQDGQ VAQTILPAYH
TAN-1	PPOPHLGVSS AASGHLGRSF LSGEPSQADV QPLGPSSLAV HTILPQ-ESP ALPTSLPSSL
Xen N	MQQQHHN-SS TTSTHINSPF CSSDISQTDL QQM-SSNNI HSVMPQ-DTQ IFAASLPSNL (
Dros N	QQQLGGLEFG SAGLDLNG-F CGSPDSFHSG QMNPPS1 QSSMSG-SSP STNMLSPSSQ
hum N	SDWSDVTTSP TPGGAGGGQR GPGTHMSEPPHNN MQVYA
TAN-1	SDWSEGVSSP PTSMQ SQIARIPEAFK
Xen N	SDWSEGISSP PT-SMQ PORTHIPEAFK
	SDWSEGVQSP AANNLYISGG HQANKGSEAIYI
)

```
-HITTPRE PLPP-IV-TF QLIPKGSIAQ PAG-
                                                                    2320
           -YQGLPSTRL ATQPHLVQTQ QVQPQNLQMQ QQNLQPANIQ QQQSLQPPPP
                                                                    2414
           -YQAMPNTRL ANQPHLMQAQ QMQQQQN----
                                                           -LQLHQS
                                                                    2384
LGIISPTGSD MGIMLAPPQS SKNSAIMQTI SPQQQQQQQQ QQQQQHQQQQ QQQQQQQQQQ
                                                                    2565
           PEST -containing Region
PFPASVGKYP TPPSQHSYAS SNAAERTPSH SGHLQGEHPY LTPSPESPDQ WSSSSPHSA-
                                                                    2433
VPPVTAAQFL !TPPSQHSY-S S-PVENTPSH QLQVP-EGPF LTPSPESPDQ WSSSSPHSNV
                                                                    2530
TQSMTTAQFL | TPPSQHSY-S S-PMDNTPSH QLQVP-DHPF LTPSPESPDQ WSSSSPHSNM
                                                                    2497
HNQQAFYQYL !TPSSQHS--- ---GGHTPQH LVQTL-D-SY PTPSPESPGH WSSSSPRSN-
                                                                    2671
                                                                    2471
                                                                    2556
                                                                    2523
                                                                    2703
```

FIG.13H

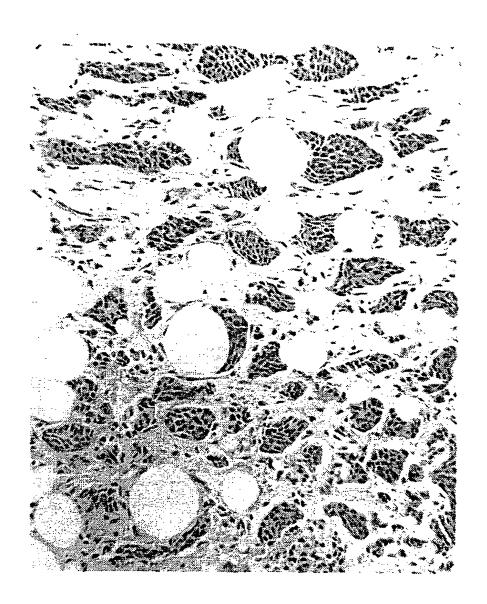


FIG.14

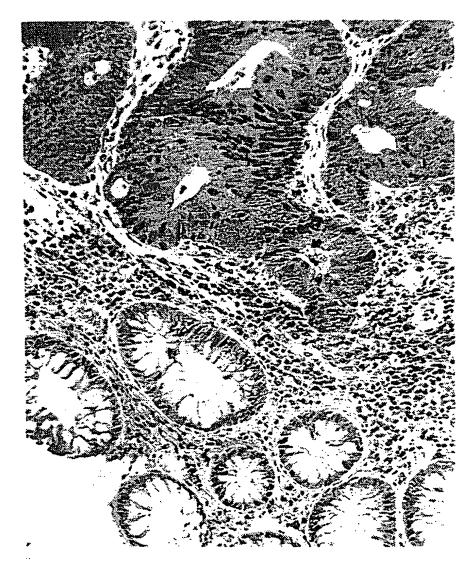


FIG. 15A

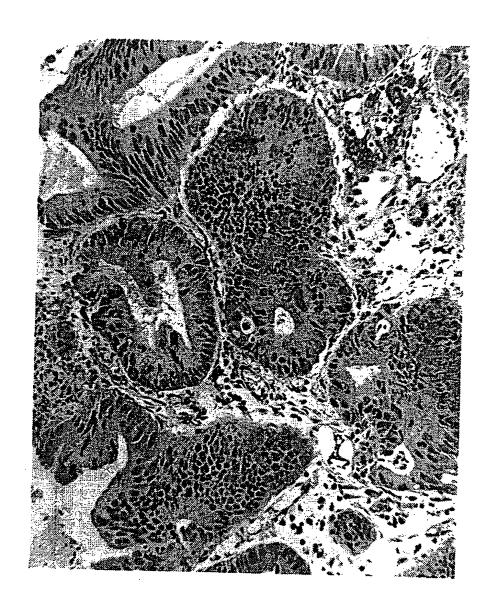


FIG. 15B

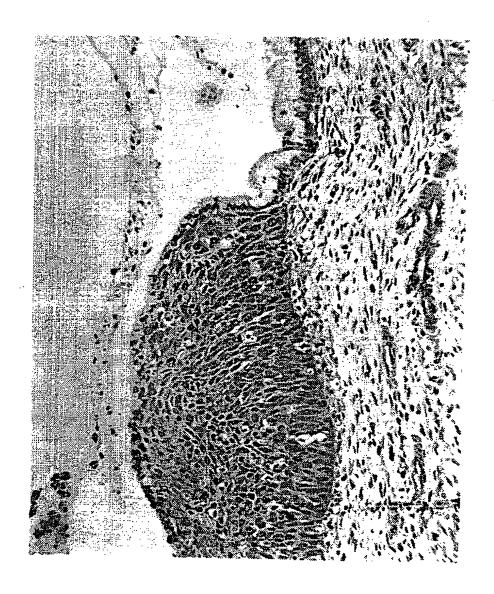


FIG. 16A

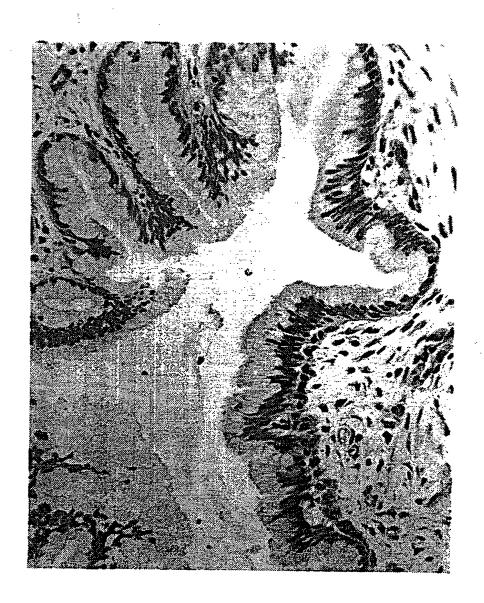


FIG. 16B

WO 94/07474 PCT/US93/09338

57/68 PALR PALL WALLAL WIC CAA PAHALOCS CGAGATGGCT ATGAACCCTG TGTAAATGAA GGAATGTGTG TTACCTACCA CAATGGCACA GGATACTGCA AATGTCCAGA AGGCTTCTTG RDG YEPC VNE GMC VIYH NGI GYC KCPE GFL> . GGGGAATATT GTCAACATCC AGACCCCTGT GAGAAGAACC GCTGCCAGAA TGGTGGGAACT TGTGTGGCCC AGGCCATGCT GGGGAAAGCC GEY CQHR DPC EKN RCQN GGT CVA QAML GKA> ACGIGCOGAT GIGCCTCAGG GITTACAGGA GAGGACTGCC AGTACTCAAC ATCTCATCCA TGCTTTGTGT CTCGACCCTG CCTGAATGGC TCR CASG FTG EDC QYST SHP CFV SRPC LNG> GGCACATGCC ATATGCTCAG COGGGATACC TATGAGTGCA CCTGTCAAGT CGGGTTTACA GGTAAGGAGT GCCAATGGAC GGATGCCTGC G T C H M L S R D T Y E C T C O V G F T G K E C O W T CTGTCTCATC CCTGTGCAAA TGGAAGTACC TGTACCACTG TGGCCAACCA GTTCTCCTGC AAATGCCTCA CAGGCTTCAC AGGGCAGAAA LSH P C A N G S T C T T V A N Q F S C K C L T G F T G Q K> TGTGAGACTG ATGTCAATGA GTGTGACATT CCAGGACACT GCCAGCATGG TGGCACCTGC CTCAACCTGC CTGGTTCCTA CCAGTGCCAG CET DVNE CDIPGH CQHG GTC LNL PGSY QCO> TGCCCTCAGG GCTTCACAGG CCAGTACTGT GACAGCCTGT ATGTGCCCTG TGCACCCTCA CCTTGTGTCA ATGGAGGCAC CTGTCGGCAG CPQ GFTG QYC DSL YVPC APS PCV NGGT CRO ACTIGGTIGACT TCACTITTIGA GTIGCAACTIC CTTCCAGGTT TIGAAGGGAG CACCTGTGAG ACGAATATTG ATGACTGCCC TAACCACAGG T C D F T F E C N C L P G F E G S T C E R N I D D C P N H R >

FIG. 17A

58/68 IGTCAGAATG GAGGGGTTTG TGTGGATGGG GTCAACACTT ACAACTGCCC CTGTCCCCCA CAATGGACAG GACAGTTCTG CACAGAGGAT CONGGVC V D G V N T Y N C R C P P Q W T G Q F C CTGGATGAAT GCCTGCTGCA GCCCAATGCC TGTCAAAATG GGGGCACCTG TGCCAACCGC AATGGAGGCT ATGGCTGTGT ATGTGTCAAC PNACQN GGTC ANR NGG YGC V C V ND CGCTGGAGTG CAGATGACTG CAGTGAGAAC ATTGATGATT GTGCCTTCGC CTCCTGTACT CCAGGCTCCA CCTGCATCGA CCGTGTGGCC G W S G D D C S E N I D D C A F A S C T P G S T C I D R V A> ICCTTCTCTT GCATGTGCCC AGAGGGGAAG GCAGGTCTCC TGTGTCATCT GGATGATGCA TGCATCAGCA ATCCTTGCCA CAAGGGGGCA S F S C M C P E G K A G L L C H L D D A C I S N P C H K G A * CTGTGTGACA CCAACCCCCT AAATGGGCAA TATATTTGCA CCTGCCCACA AGGCTACAAA GGGGCTGACT GCACAGAAGA TGTGGATGAA LCD INPL NGQ YIC TCPQ GYK GAD CTED IGIGCCATCG CCAATAGCAA ICCITGIGAG CAIGCAGGAA AAIGIGIGAA CACCGATGCC GCCTICCACT GIGAGIGICI GAACCGITAT CAM ANSN PCE HAG KCVN TDG AFH CECL GCAGGACCTC GTTGTGAGAT GGACATCAAT GAGTGCCATT CAGACCCCTG CCAGAATGAT GCTACCTGTC TGGATAAGAT TGGAGGCTTC AGPRCEMDINECH SDPC QND ATC LDKI GGF> ACATGICIGI GCAIGCCAGG ITTCAAAGGI GIGCATIGIG AATTAGAAAT AAATGAATGI CAGAGCAACC CITGIGIGAA CAATGGGCAG TCL CMPG FKG VHC ELEINEC QSN PCVN NG Q>

FIG.17B

IGIGIGGATA AAGICAATCC TITICCAGIGC CIGIGICCIC CIGGITICAC IGGGCCAGIT IGCCAGATIG ATATIGATGA CIGITICCAGI C V D K V N R F Q C L C P P G F T G P V C Q I D I D D C S S>

59/68 ACTOCCTIGIC TIGALTICISCE AMAGISTATIC GATCACCOCA ATGCCTATGA ATGCCAGTGT GCCACAGGTT TCACTGGTGT GTTGTGTGAG TPC LNG A KCI DHP NG Y E CQC A TG F TG V LCE> GAGAACATIC ACAACIGIGA CCCCGATCCT IGCCACCATG GICAGTGICA GGATGGTATT GATTCCTACA CCTGCATCTG CAATCCCGGG ENIDNOD PDP CHH GQCQ DGI DSY TCIC NPG> TACATGGGC CCATCIGCAG IGACCAGATT GATGAATGTT ACAGCAGCCC TIGCCTGAAC GATGGTCGCT GCATTGACCT GGTCAATGGC Y M G A I C S D Q I D E C Y S S P C L N D G R C I D L -1950 TACCAGTGCA ACTGCCAGCC AGGCACGTCA GGGGTTAATT GTGAAATTAA TTTTGATGAC TGTGCAAGTA ACCCTTGTAT CCATGGAATC Y Q C N C Q P G T S G V N C E I N F D D C A S N P C I H G I> IGTATGGATG GCATTAATCG CTACAGTTGT GTCTGCTCAC CAGGATTCAC ACCGCAGAGA TGTAACATTG ACATTGATGA GTGTGCCTCC CMD GINRYSC VCS PGFT GQR CNI DIDE CAS AATCCCTGTC GCAAGGGTGC AACATGTATC AACGGTGTGA ATGGTTTCCG CTGTATATGC CCCGAGGGGAC CCCATCACCC CAGCTGCTAC N.P.C. RKGATCING VNGFRCIC PEG PHHPSCYS TCACAGGTGA ACGAATGCCT GAGCAATCCC TGCATCCATG GAAACTGTAC TGGAGGTCTC AGTGGATATA AGTGTCTCTG TGATGCAGGC S Q V N E C L S N P C I H G N C T G G L S G Y K C L C TGGGTTGGCA TCAACTGTGA AGTGGACAAA AATGAATGCC TTTCGAATCC ATGCCAGAAT GGAGGAACTT GTGACAATCT GGTGAATGGA WVG INCE VDK NECLSNP CQN GGT CDNL VNG>

FIG.17C

SUBSTITUTE SHEET (RULE 26)

TACAGGIGIA CTIGCAAGAA GGCCTITAAA GGCTATAACT GCCAGGIGAA TATIGATGAA TGTGCCTCAA ATCCATGCCT GAACCAAGGA
YRCTCKFGFKGYNCQVNIDECASNPCLNQG>

WO 94/07474 PCT/US93/09338

60/68 ACCTGCTTTG ATGACATAAG TGGCTACACT TGCCACTGTG TGCTGCCATA CACAGGCAAG AATTGTCAGA CAGTATTGGC TCCCTGTTCC T C F D D I S G Y T C H C V L P Y T G K N C Q T V L A CCAAACCCTT GIGAGAATGC IGCTGTTIGC AAAGAGTCAC CAAATTTIGA GAGTTATACT IGCTIGTGTG CTCCTGGCTG GCAACGTCAG PNP CENAAVCKES PNFE SYT CLC APG W Q G O> CGGTGTACCA TIGACATIGA CGAGTGTATC TCCAAGCCCT GCATGAACCA TGGTCTCTGC CATAACACCC AGGGCAGCTA CATGTGTGAA RCTIDIDECISKP CMNH GLC HNT OGSY MCE> TGTCCACCAG GCTTCAGTGG TATGGACTGT GAGGAGGACA TTGATGACTG CCTTGCCAAT CCTTGCCAGA ATGGAGGTTC CTGTATGGAT CPPGFSG MDCEED IDDC LAN PCQ NGGS CMD> GGAGTGAATA CITICTCCTG CCICTGCCTT CCGCGTTTCA CTGGGGATAA GTGCCAGACA GACATGAATG AGTGTCTGAG TGAACCCTGT G V N T F S C L C L P G F T G D K C Q T D M N E C L S AAGAATGGAG GGACCTGCTC TGACTACGTC AACAGTTACA CTTGCAAGTG CCAGGCAGGA TTTGATGGAG TCCATTGTGA GAACAACATC KNG GTCS DYV NSY TCKC QAG FDG V H C E . AATGAGTGCA CIGAGAGCTC CTGTTTCAAT GGTGGCACAT GTGTTGATGG GATTAACTCC ITCTCTTGCT TGTGCCCTGT GGGTTTCACT NECTESS CFN GGT CVDG INS FSC LCPV GFT> GGATCCTTCT GCCTCCATGA GATCAATGAA TGCAGCTCTC ATCCATGCCT GAATGAGGGA ACGTGTGTTG ATGGCCTGGG TACCTACCGC G S F C L H E I N E C S S H P C L N E G T C V D G L G TGCAGCTGCC CCCTGGGCTA CACTGGGAAA AACTGTCAGA CCCTGGTGAA TCTCTGCAGT CGGTCTCCAT GTAAAAACAA AGGTACTTGT. CSC PLGY TGK NCQ TLVN LCS RSP CKNK GTC>

FIG.17D

											61,	/6	В															
	3	250			326)		3270)		328	0		32	90)		3300)		331	0		3.	320		3.	330
CTT	C1C1	*		001				*		\T~		*		DO 6	*		AT.	*		~~~		*			*			*
					E ?		AGIG D C		10	אנג זיינ	CATCTO S	نا نا م	AIG W	GGC1	UU C	IGC	CIA	HGI			GCCC. P		IGT V		FTG C			
•	ų,	IX.	N	Λ	L ,	, (, (Ĺ	•	, ;	J	U	**	^.	U	^	'	U	U	•	F	14	٧	3	L	U	İ	A)
	3.	340			3350)		3360)		3370	0		33	80		•	3390			340	0		34	110		34	120
		*			4	:						•			*			*							-			*
											CCAG																	
А	2 1	Κ	K	G	Vι	٠ ،	/ t	Н	L	. (Q	Н	2	G	٧	C	i	N	Α	G	N	ı	H	Y	C	Q	С	P>
	34	430			3440)		3450			3460)		34	70		3	3480			3490)		35	600		35	510
		*									•										4	;			*			*
											CCATO																	
L	G	ſ	1	G	SY	, C	: E	E	Q) L	D	Ε	C	A	S	N	Р	C	Q	Н	G	A	Ī	C	S	D	F	>
	35	520			3530	ì		3540			3550)		356	50		3	570			3580)		35	90		35	200
	•	*			*		,	*			3330			551				*			*			JJ	*		JU	
GGTG	GATA	\CA	GA	TGC	CAGTG	TGT	CCC	AGGC	TA	TCA	CCCTC	; T(CAAC	TGTO	À	GTAT	GAA	GTG	GAT	[GAC	TGCC	: AG	AA1	CAG	CC	CTGC		-
					E C		Р				G					Y				E						C		
	36	10			3620			3630			3640	1		360	'n		3	660			3670	1		36	ጸስ		36	٥n
		*			\$		•	*			*	,		Ų0.	*		J	*			*			JU	*		30	
GGAG	GCAC	CT	GT	ATTO	SACCT	TGT	GAA(CAT	TT	CAA	GTGCT	CT	TGC	CCAC	C	ACCC	ACT	CCC	GGC	CTA	CTCT	GT	GAA	GAG	AA	CATTO	GATG	AC
G	G I		C	I	DL	٧	N	Н	F	K	C	S	C	P	P	G	Ţ	R	G	L	L	C	E	E	N	I	D 1	D>
	37	00			3710		7	720			3730			374	n		τ.	75N			3760			37	70		378	00
	3,	*			J/ 10 #		٠	*			3/30				*		J	, JU *			J/UU *			JI.	/U *		3/	0U غ
TGTG	α	GC (GTO	CCC	ATTG	CCT	TAAT	CCT	GG	TCA	GTGCA	TG	GAT.	AGGA	Ţ	TGGA	GGC.	TAC	AGT	TGT	CCCT	GC	TTG	CCT(X	CTTT	CTG	œ
C	A R	(G	Ρ.	H C	L	N	G	G	Q	C	M	D	R	ĺ	G	G	Y	Ş	C	R	C	L	P	G	F	A (G>
	37	90			3800		7	01A			3820			707	۸		70	240			70EN			701	٠,		70	70
	37	3 ∪ ‡			J000 *		J	*			J02U #				U ‡		J()4U *			3850			386)U		387	/U
GAGC	GTTG	TG /	AGG	GAG	ACAT	CAAC	CAC	TGC	CTC	CTCC	CAACC	CC	TGC	AGCT	C .	TGAG	GGC/	VGC I	CTG	GAC	TGTA	TAC	CAG	CTCA	VC 1	CAATO	ACT/	AC
E F	R C	1	:	G	l d	N	E	C	L	S	N	Ρ	C	S	S	Ε	G	S	L	D	C	I	Q	L	T	N	D Y	(>
	700	20			7000		7	000			7010			700	^		70	70			70.40			305			700	
	200	DU ±			7020		J	300			3910			3921	U		25	120		•)94U			395	Û		396	
CTGTG	CTGTT																										CCAC	* 'T
L C	. V	C	,	R :	S A	F	1	G	R	Н	C	E	T	F۱	,	D	۷.	C	P	Q	M	р Р	C	L	N	G	G T	'' '>
											4000									Į.								
TGTGC											* TGCC								ייינוני							ידרידר		
											C																	

FIG.17E

SUBSTITUTE SHEET (RULE 26)

62/68 GTGAAATGTA GGAAGGGGGA GCAGTGTGTG CACACCGCCT CTGGACCCCG CTGCTTCTGC CCCAGTCCCC GGGACTGCGA GTCAGGCTGT VKC RKGE QCV HTA SGPR CFC PSP RDCF SGC> GCCAGTAGCC CCTGCCAGCA CGGGGGCAGC TGCCACCCTC AGCGCCAGCC TCCTTATTAC TCCTGCCAGT GTGCCCCACC ATTCTCGGGT ASS PCQHGGS CHPQRQPPYY SCQ CAPPFS G> AGCCGCTGTG AACTCTACAC GGCACCCCCC AGCACCCCTC CTGCCACCTG TCTGAGCCAG TATTGTGCCG ACAAAGCTCG GGATGGCGTC SRC ELY TAPP STPPATCLSOY CADKARDG V> TGTGATGAGG CCTGCAACAG CCATGCCTGC CAGTGGGATG GGGGTGACTG TTCTCTCACC ATGGAGAACC CCTGGGCCAA CTGCTCCTCC C D E A C N S H A C Q W D G G D C SLIMENPWAN CCACTICCCT GCTGGGATTA TATCAACAAC CAGTGTGATG AGCTGTGCAA CACGGTCGAG TGCCTGTTTG ACAACTTTGA ATGCCAGGGG PLP CWDY INN QCD ELCN TVE CLF DNFE CQG> AACAGCAAGA CATGCAAGTA TGACAAATAC TGTGCAGACC ACTTCAAAGA CAACCACTGT AACCAGGGGT GCAACAGTGA GGAGTGTGGT NSK TCKY DKY CAD HFKD NHC NQG CNSE ECG> TGGGATGGGC TGGACTGTGC TGCTGACCAA CCTGAGAACC TGGCAGAACG TACCCTGGTT ATTGTGGTAT TGATGCCACC TGAACAACTG W D G L D C A A D Q P E N L A E G T L V I V V L M P P CTCCAGGATG CTCGCAGCTT CTTGCGGGCA CTGGGTACCC TGCTCCACAC CAACCTGCGC ATTAAGCGGG ACTCCCAGGG GGAACTCATG L Q D A R S F L R A L G T L L H T N L R I K R D S Q G GTGTACCCCT ATTATGGTGA GAAGTCAGCT GCTATGAAGA AACAGAGGAT GACACGCAGA TCCCTTCCTG GTGAACAAGA ACAGGAGGTG V Y P Y Y G E K S A A M K K Q R M T R R S L P G E Q E Q E V>

FIG.17F

SUBSTITUTE SHEET (RULE 26)

63/68 GCTGGCTCTA AAGTCTTTCT GGAAATTGAC AACCGCCAGT GTGTTCAAGA CTCAGACCAC TGCTTCAAGA ACACGGATGC AGCAGCAGCT AGS KVFLEID NRQ CVQD SDH CFK NIDA AAA CTCCTGGCCT CTCACGCCAT ACAGGGGACC CTGTCATACC CTCTTGTGTC TGTCGTCAGT GAATCCCTGA CTCCAGAACG CACTCAGCTC LLA SHAI QGT LSY PLVS VVS ESL TPER TO 1> CTCTATCTCC TIGCTGTTGC TGTTGTCATC ATTCTGTTTA TTATTCTGCT GGGGGTAATC ATGGCAAAAC GAAAGCGTAA GCATGGCTCT LYLLAVA VVIILFIILL GVI MAKRKRK H G S> CTCTGGCTGC CTGAAGGTTT CACTCTTCGC CGAGATGCAA GCAATCACAA GCGTCGTGAG CCAGTGCGAC AGGATGCTGT GGGGCTGAAA LWL PEGFTLR RDASNHK RRE PVG QDAV GLKS AATCTCTCAG TGCAAGTCTC AGAAGCTAAC CTAATTGGTA CTGGAACAAG TGAACACTGG GTCGATGATG AAGGGCCCCCA GCCAAAGAAA NLS VQVS EAN LIG TGTS EHW VDD EGPQ PKK GTAAAGGCTG AAGATGAGGC CTTACTCTCA GAAGAAGATG ACCCCATTGA TCGACGGCCA TGGACAGAGC AGCACCTTGA AGCTGCAGAC V K A E D E A L L S E E D D P I D R R P W T Q Q H L E ATCCGTAGGA CACCATCGCT GCCTCTCACC CCTCCTCAGG CAGAGCAGGA GGTGGATGTG TTAGATGTGA ATGTCCGTGG CCCAGATGGC IRR TPS LALT PPQ A EQE V D V L D V N V R G P D G> IGCACCCCAT IGATGTIGGC LICICICCGA GGAGGCAGCT CAGATTIGAG IGATGAAGAT GAAGATGCAG AGGACTCTIC IGCTAACATC CTPLMLASLR GGS SDLS DED E DA E DSS AN I>

FIG.17G

SUBSTITUTE SHEET (RULE 26)

ATCACAGACT TGGTCTACCA GGGTGCCAGC CTCCAGGCCC AGACAGACCG GACTGGTGAG ATGGCCCTGC ACCTTGCAGC CCCCTACTCA

64/68 CGGCCTGATG CTGCCAAGCG TCTCCTGGAT GCAGGTGCAG ATGCCAATGC CCAGGACAAC ATGGGCCGCT GTCCACTCCA TGCTGCAGTG RAD AAKR LLD AGA DANA Q DN M G R C P L H GCAGCTGATG CCCAACGTGT CTTCCAGATT CTGATTCGCA ACCGAGTAAC TGATCTAGAT GCCAGGATGA ATGATGGTAC TACACCCCTG AAD AQGV FQILIR NRVT DLD ARM NDGT TPL> ATCCTGGCTG CCCCCCTGGC TGTGGAGGGA ATGGTGGCAG AACTGATCAA CTGCCAAGCG GATGTGAATG CAGTGGATGA CCATGGAAAA ILAARLA VEG MVAELIN CQA DVN AVDD HGK> TCTGCTCTTC ACTGGGCAGC TGCTGTCAAT AATGTGGAGG CAACTCTTTT GTTGTTGAAA AATGGGGGCCA ACCGAGACAT GCAGGACAAC SALHWAA AVN NVE ATLL LLK NGA NRDM QD N> AAGGAAGAGA CACCTCTGTT TCTTGCTGCC CGGGAGGGGA GCTATGAAGC AGCCAAGATC CTGTTAGACC ATTTTGCCAA TCGAGACATC KEETPLF LAAREG SYEAAKI LLD HFAN ACAGACCATA TOGATOGTOT TOCCOGGGAT GTGGCTCGGG ATCGCATGCA CCATGACATT GTGCCCCTTC TGGATGAATA CAATGTGACC TOH MORE PRO VAR DRMH H DI VRELDEY NV T> . CCAAGCCCTC CAGGCACCGT GTTGACTTCT GCTCTCTCAC CTGTCATCTG TGGGCCCAAC AGATCTTTCC TCAGCCTGAA GCACACCCCA PSPPGTVLTS ALS PVIC GPN RSFLSLK HTP> ATGGGCAAGA AGTCTAGAGG GCCCAGTGCC AAGAGTACCA TGCCTACTAG CCTCCCTAAC CTTGCCAAGG AGGCAAAGGA TGCCAAGGGT M G K K S R P S A K S T M P T S L P N L A K E A K D AGTAGGAGGA AGAAGTCTCT GAGTGAGAAG GTCCAACTGT CTGAGAGTTC AGTAACTTTA TCCCCTGTTG ATTCCCTAGA ATCTCCTCAC

FIG.17H

SUBSTITUTE SHEET (RULE 26)

S R R K K S L S E K V Q L S E S S V T L S P V D S L E S P H>

65/68 ACGTATGTTT CCGACACCAC ATCCTCTCCA ATGATTACAT CCCCTGGGAT CTTACAGGCC TCACCCAACC CTATGTTGGC CACTGCCGCC TYV SDTI SSP MIT SPGILQA SPN PMLATAA CCTCCTGCCC CAGTCCATGC CCAGCATGCA CTATCTTTT CTAACCTTCA TGAAATGCAG CCTTTGGCAC ATGGGGCCAG CACTGTGCTT PPAPVHAQHALSF SNLHEMQ PLAHGAS TVL> CCCTCAGTGA GCCAGTTGCT ATCCCACCAC CACATTGTGT CTCCAGGCAG TGGCAGTGCT GGAAGCTTGA GTAGGCTCCA TCCAGTCCCA PSV SQLL SHH HIV SPGS GSA GSL SRLH PVP GTCCCAGCAG ATTGGATGAA CCGCATGGAG GTGAATGAGA CCCAGTACAA TGAGATGTTT GGTATGGTCC TGGCTCCAGC TGAGGGCACC VPADWMNRME VNE TQYNEMF GMV LAPAE.GT> CATCCTGGCA TAGCTCCCCA GAGCAGGCCA CCTGAAGGGA AGCACATAAC CACCCCTCGG GAGCCCTTGC CCCCCATTGT GACTTTCCAG HPG IAPQ SRPPEG KHIT TPR EPL PPI V CTCATCCCTA AAGGCAGTAT TGCCCAACCA GCGGGGCTC CCCAGCCTCA GTCCACCTGC CCTCCAGCTG TTGCGGGCCC CCTGCCCACC LIPKGSI AQPAGA PQPQ STC PPA VAGP ATGTACCAGA TICCAGAAAT GGCCCGTTTG CCCAGTGTGG CTTTCCCCAC TGCCATGATG CCCCAGCAGG ACGGGCAGGT AGCTCAGACC MYQ IPEM ARL PSV AFPT AMM PQQ DGQV AQT> ATTCTCCCAG CCTATCATCC TITCCCAGCC TCTGTGGGCA AGTACCCCAC ACCCCCTICA CAGCACAGTT ATGCTTCCTC AAATGCTGCT ILP AYHP FPA SVG KYPT PPS QHS YASSNAA GAGCGAACAC CCAGTCACAG TGGTCACCTC CAGGGTGAGC ATCCCTACCT GACACCATCC CCAGAGTCTC CTGACCAGTG GTCAAGTTCA ERT PS H S G H L Q G E H P Y L T P S P E S P D Q W S S S>

FIG. 171

7700	7740	7700	7770	7740	7750	7360	7370	7380
7300	7310 *	7320 *						*
	CTGCTTCTGA S A S D	CTGGTCAGAT W S D	GTGACCACCA V T T	GCCCTACCCC S P T P	TCCCCGTCCT G G A	GGAGGAGGTC G G G	AGCGGGGACC Q R G P	TGGGACACAC G T H>
7390	7400	7410	7420				7460	7470
	CACCACACAA P P H N		GTTTATGCGT V Y A>	GAGAGAGTCC			ACTGACTTTT	GTAAATGCTG
7480	7490	7500					7550	7560
CTGAGGAACA	AATGAAGGTC	ATCCGGGAGA	GAAATGAAGA				AAGAGAAGAT	GITCTTATIC
7570	7580		7600					7650 •
AGATAATGCA	AGAGAAGCAA			TCTGCAAGGC		TICTAATCTA	ATAAGACAAG	
7660	7670	7680		7700		7720	7730	7740
* TGCAAGATGA	ATACAAGCCT	TGGGTCCATG	TITACTCTCT	* ICTATTIGGA		GATGCTTATT	GAAGCCCAGA	CATTCTTGCA
7750	7760	7770	7780	7790				
GCTTGGACTG	* CATTTTAAGC	CCTGCAGGCT	TCTGCCATAT			-	TGGGAATTAT	
7840	7850	7860		7880				7920
TCTGCCTGAA	TTGACCTACG	CATCTCCTCC		TICTITIGIC			TIGCACCTCT	CCCTGATTGT
7930	7940	7950	7960	7970	7980	7990	8000	8010
AGCCCTACCA	GCATGTTATA	GGGCAAGACC	TTTGTGCTTT	IGATCATICT	GGCCCATGAA	ACCAACTTIG	GICICCITIC	CCCTCCTGTC
8020	8030	8040	8050	8060	8070	8080	8090	8100
TICCCCGTAT							TIGITICITI	GGAAAATGGA
8110							8180 *	
CATACTGTAT								GGGCAGGAGA
8200	8210	8220	8230	8240	8250	8260	8270 •	8280
TCCCTTCAAG	AGGCTGCACC						AAGGGTGTGA	

FIG. 17J SUBSTITUTE SHEET (RULE 26)

				67/68				
829	930	8310						8370
TTTCTGTGT	A TOGGCCTGG	T CAGTGTAAAG	TITTATCCTI	GATAGTCTAC	TTACTATGAC	CCTCCCCAC	*	CAGAAAAAGG
8380	839	0 8400					0 8450	8460
TTTGGAATG	TGGAATGAC	* C AAGAGACAAG			TTACCCACC		CTACTICCTG	CCAAGCATTC
8470	848	0 8490	8500			8530	8540	8550
CATTGACTGO		* A CACATTIGIC			•		* C AGCATATGAA	ACTAGTCTTA
8560		0 8580						
ACTGTTGAGC	CTITCCTIT	* *C ATATCCACAG	AAGACACTGT	CTCAAATGTT	GTACCCTTGC	CATTTAGGAC	TGAACTTTCC	TTAGCCCAAG
8650	8660	8670						8730
GGACCCAGTG	ACAGTTGTCT	TCCGTTTGTC			TIATCTICCT			ATCITICITI
8740	8750						8810	8820
CACACCGTGT	CCTCCCTGTT	ACTGGTATAC	CCAGTATGTT (* TTGGAAAGTT
8830	8840	8850						
GGACTIGTTT	TCTATGATCC	AAAACAGCCC	TATAAGAAGG 1	TGGAAAAGG	AGGAACTATA	TAGCAGCCTT	TGCTATTTTC	TGCTACCATT
8920	8930	8940	8950	8960	8970	8980	8990	9000
TCTTTTCCTC	TGAAGCGGCC	ATGACATTCC (•		ACTCAACAGA	ACATTTTCCT	TTCCTAGAGT (CACCTTTTAG
9010		9030					9080	9090
ATGATAATGG .	* ACAACTATAG	ACTTGCTCAT T	GTTCAGACT G				ATTCATGCTC 1	TTGCCAATTT
9100	9110	9120					9170	9180
CTTTGACTTT	* CTTTTAAGGG	CAGAAGCATT T	TAGTTAATT G	TAGATAAAG A	ATAGITITC 1	TCCTCTTCT	CCTTGGGCCA G	* TTAATAATT
9190	9200	9210	9220	9230	9240	9250	9260	9270
GGTCCATGGC 1	ACACTGCAA	CTTCCGTCCA G	TGCTGTGAT GC	CCATGACA C	CTGCAAAAT A	AGTTCTGCC 1	GGGCATTII G	* TAGATATTA

FIG.17K

SUBSTITUTE SHEET (RULE 26)

				68/68				
9280	9290	9300	9310	9320	9330	9340	9350	9360
9200				•	•		•	
ACAGGTGAAT	TCCCGACTCT	TTTGGTTTGA	ATGACAGTTC	TCATTCCTTC	TATGGCTGCA	AGTATGCATC	AGTGCTTCCC	ACTTACCTGA
9370	9380	9390	9400	9410	9420	9430	9440	9450
•							711707740	CALATTTATT
THIGHCIGIC	GGTGGCCCCA	TATCGAAACC	CTCCCTGTCT	GTTGGCATAA	TAGTTTACAA	AIGGIIIIII	CAGTCCTATC	CAMILIAII
9460	9470	9480	9490	9500	9510	9520	9530	9540
							*	•
GAACCAACAA	AAATÄATTAC	TTCTGCCCTG	AGATAAGCAG	ATTAAGTTTG	TICATICTCT	GCTTTATTCT	CTCCATGTGG	CAACATTCTG
9550	9560	9570	9580	9590	9600	9610	9620	9630
	_		•				*	*
TCAGCCTCTT	TCATAGTGTG	CAAACATTTT	ATCATTCTAA	ATGGTGACTC	ICIGCCCTIG	GACCCATTTA	TTATTCACAG	ATGGGGAGAA
9640	9650	9660	9670	9680	9690	9700	9710	9720
				. +		*	*	T 1 1 0 0 0 7 0 0 0 0
CCTATCTGCA	TOGACCETCA	CCATCCTCTC	TGCAGCACAC	ACAGTGCAGG	GAGCCAGTGG	CGATGGCGAT	GACTITICITO	CCCIGGGAAT
TCC								

FIG.17L

INTERNATIONAL SEARCH REPORT

International application No. PCT/US93/09338

			101/03/3/09.	,,,,
IPC(5) US CL	ASSIFICATION OF SUBJECT MATTER: Please See Extra Sheet.: 424/85.8; 435/6; 514/1, 2, 24 to International Patent Classification (IPC) or to bo	th national classification	and IPC	
	LDS SEARCHED			
Minimum o	documentation searched (classification system follow	ed by classification sym	bols)	
U.S. :	424/85.8; 435/6; 514/1, 2, 24			
Documenta	tion searched other than minimum documentation to t	he extent that such docum	nents are included	d in the fields searched
	data base consulted during the international search (name of data base and, v	where practicable	, search terms used)
C. DOC	CUMENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where	appropriate, of the releva	ant passages	Relevant to claim No.
Y	US, A, 5,115,096 (SHOYAB ET AL) lines 12-27, column 11, lines 39-6 columns 16-18, column 28, Table IV	53, column 14, 1	e column 8, ines 16-68,	1-18, 22-28, 31, 34-40, 42-52, 55-58, 63-67, 75-94
A	US, A, 5,132,212 (KIRSCH ET AL) lines 25-36.	21 JULY 1992, se	e column 7,	23-31, 45, 55-60, 63-67, 84-90
A,E	US, A, 5,264,557 (SALOMON ET A column 1, lines 20-49.	L) 23 NOVEMBE	R 1993, see	1-18,22-28,31,34- 40,42-52,55- 58,63-67,75-94
X Furth	er documents are listed in the continuation of Box (See patent	family annex.	
	cial estegories of cited documents; ument defining the general state of the art which is not considered	date and not in co	aflict with the applica	mational filing date or priority tion but cited to understand the
to b	e part of particular relevance		ry underlying the inve ticular relevance: the	ntion claimed invention cannot be
'L' doc	ier document published on or after the international filing date ument which may throw doubts on priority claim(s) or which is		or cannot be consider	ed to involve an inventive step
cites	d to establish the publication date of another citation or other citation (as specified)	"Y" document of par	ticular relevance; the	claimed invention cannot be
O° doce	ament referring to an oral disclosure, use, exhibition or other	combined with or	ivolve an inventive se or more other such a person skilled in the	step when the document is documents, such combination
P* doct	ment published prior to the international filing date but later than priority date claimed		r of the same patent i	i
Date of the a	ctual completion of the international search er 1993	Date of Gnathing of the	injernational sear	ch report
Commissions Box PCT	ailing address f the ISA/US er of Patents and Trademarks	Authorized officer STEPHEN WALSH	D.76	ryza for
Washington,	D.C. 20231 NOT APPLICABLE	Telephone No. (703)	-	

Form PCT/ISA/210 (second sheet)(July 1992)*

YOCID- -WO 940747461 I -

INTERNATIONAL SEARCH REPORT

International application No. PCT/US93/09338

	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Category*	THE NEW BIOLOGIST, Volume 2, No.7, issued July 1990, R.J. Greenspan, "The Notch Gene, Adhesion, And Developmental Fate In The Drosophila Embryo", pages 595-600, see abstract.	1-18,22- 28,31,34-40,42- 52,55-58,63- 67,75-94 1-94
A	CELL, Volume 67, issued 15 November 1991, I. Rebay et al, "Specific EGF Repeats of Notch Mediate Interactions with Delta and Serrate: Implications for Notch as a Multifunctional Receptor", pages 687-699, see entire document.	1-94
A,P	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, Volume 90, issued May 1993, J.F. De Celis et al, "Genetic and molecular characterization of a Notch mutation in its Delta- and Serrate-binding domain in <u>Drosophila</u> ", pages 4037-4031, see page 4037, column 2, paragraph 2.	21,54
A	EUROPEAN JOURNAL OF BIOCHEMISTRY, Volume 190, issued May 1990, J.A. Campos-Ortega et al, "Molecular analysis of a cellular decision during embryonic development of <u>Drosophila melanogaster</u> : epidermogenesis or neurogenesis", pages 1-10, see section bridging pages 4-5, page 8, column 2, paragraphs 2 and 4.	1-20,22,34- 40,42-44,46- 53,75-83,91-94
A	Biological Abstracts, Volume 93, No.11, issued 01 June 1992, J. Robbins et al, "Mouse mammary tumor gene int-3: A member of the notch gene family transforms mammary epithelial cells", see page AB-465, abstract no. 122736, J. Virol., 66(4), 2594-2599.	23-28,31,45,55- 58,63-67,84-90
A	CELL, Volume 66, issued 23 August 1991, L.W. Ellisen et al, "TAN-1, the Human Homolog of the Drosophila Notch gene, Is Broken by Chromosomal Translocations in T Lymphoblastic Neoplasms", pages 649-661, see pages 657-658.	1-18,22- 28,31,34-40,42- 52,55-58,63- 67,75-94

INTERNATIONAL SEARCH REPORT

Inte. .ional application No. PCT/US93/09338

A. CLASSIFICATION OF SUBJECT MATTER: IPC (5):

A61K 31/00, 31/70, 37/02, 39/44, 39/395; C07H 21/04; G01N 33/53, 33/68

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, BIOSIS, CA, INPADOC, JICST-E, MEDLINE, search terms: notch protein or gene product, delta protein or gene product, serrate protein or gene product, disease, disorder, cancer, DNA, nucleic acid, anti-sense, therapy or treatment or pharmaceutical

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

- I. Claims 1-18, 22, 34-40, 42-44, 46-52, 75-83 and 91-94, drawn to pharmaceutical compositions comprising a Notch protein, fragments, chimeras, derivatives or analogs of a Notch protein, methods of treating or preventing malignancy or nervous system disorder, a method of promoting tissue regeneration or repair, and a method of treating a benign dysproliferative disorder, classified in Class 514, subclass 2.
- II. Claims 19, 20 and 53, drawn to a pharmaceutical composition comprising a derivative or analog of a Delta protein and a method of treating or preventing a malignancy, classified in Class 514, subclass 2.
- III. Claims 21 and 54, drawn to a pharmaceutical composition comprising a derivative or analog of a Serrate protein, classified in Class 514, subclass 2.
- IV. Claims 23-28, 31, 45, 55-58, 63-67 and 84-90, drawn to a pharmaceutical composition comprising a nucleic acid encoding a Notch protein, fragments or chimeras of a Notch protein, a method of treating or preventing malignancy comprising administration of nucleic acid encoding a Notch protein, a method of treating a patient with a tumor, and a pharmaceutical composition comprising an isolated oligonucleotide consisting of at least six nucleotides and a recombinant cell, classified in Class 514, subclass 44.
- V. Claims 29 and 59, drawn to a pharmaceutical composition comprising nucleic acid encoding a fragment of a Delta protein, and a method of treating or preventing malignancy comprising administration of nucleic acid encoding a Delta protein, classified in Class 514, subclass 44.
- VI. Claims 30 and 60, drawn to a pharmaceutical composition comprising nucleic acid encoding a fragment of a Serrate protein, and a method of treating or preventing malignancy comprising administration of nucleic acid encoding a Serrate protein, classified in Class 514, subclass 44.
- VII. Claims 32, 33, 41, 61 and 62, drawn to a pharmaceutical composition comprising an antibody and a method of treating or preventing malignancy comprising administration of antibody, classified in Class 424, subclass 85.8.
 - VIII. Claim 68-74, drawn to a method of diagnosing a disease, classified in Class 435, subclass 6.

Form PCT/ISA/210 (extra sheet)(July 1992)*

in the contract of the comment of the comment of the comment of the contract o and the second of the second o